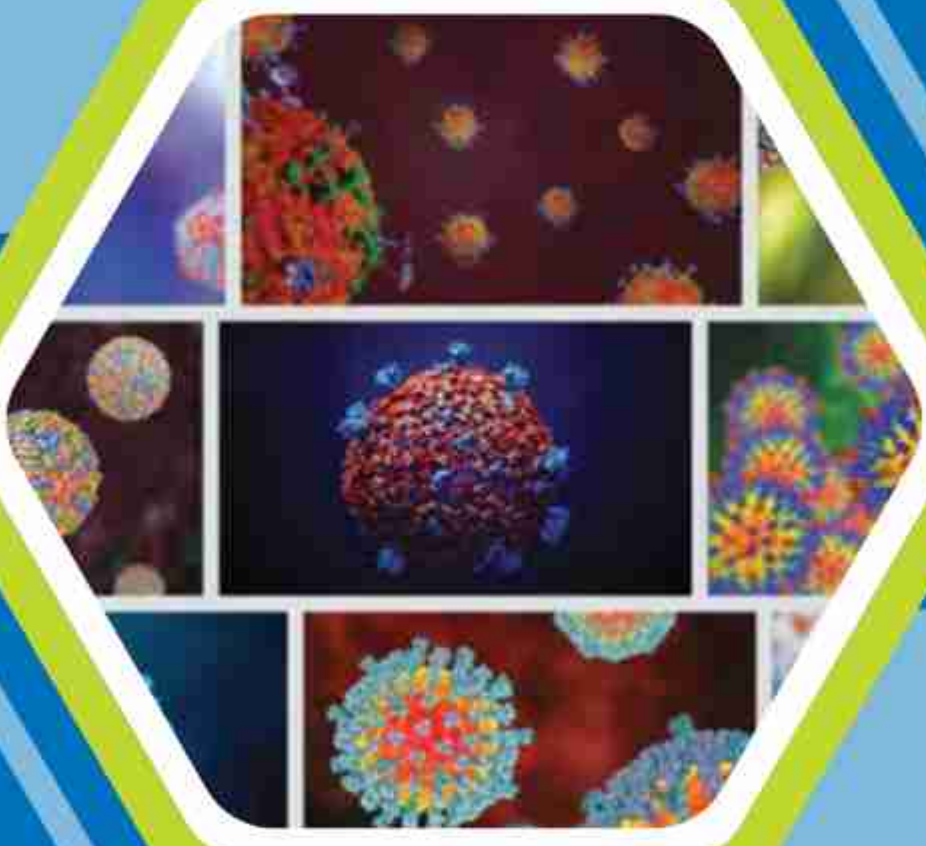
NATIONAL GUIDELINE FOR AFP AND VACCINE PREVENTABLE DISEASES SURVEILLANCE BANGLADESH



Expanded Programme on Immunization (EPI)
Directorate General of Health Services (DGHS)
Mohakhali, Dhaka-1212, Bangladesh

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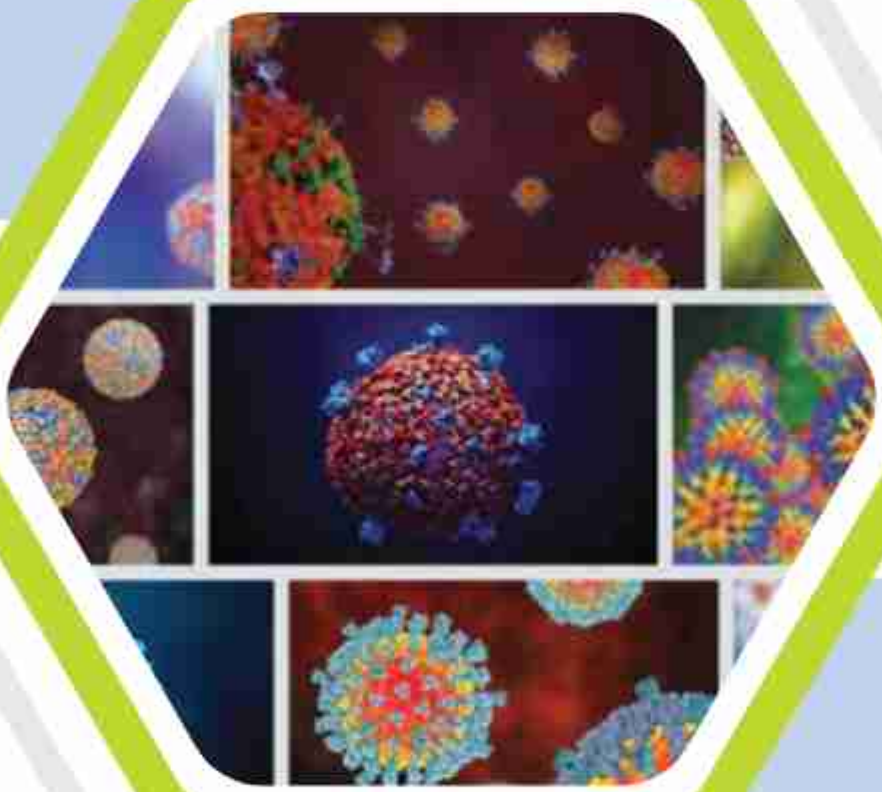

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MESSAGE

Bangladesh has made tremendous progress in the fight against Vaccine Preventable Diseases (VPDs) over the last decades. The country has been certified as polio free by the World Health Organization. The number of deaths due to other VPDs has also notably reduced to one digit, even zero. Such remarkable success shows that the country is on track as it envisages to protect all eligible beneficiaries from VPDs.

Attaining zero cases of VPDs or public health elimination, and zero deaths due to VPDs will take efforts beyond business-as-usual, and surveillance is pivotal for it. This manual underlines the strategies and guidelines regarding VPDs surveillance.

Robust surveillance and M&E will continue to be emphasized as one of the core interventions in Expanded Programme on Immunization (EPI). Use of surveillance data is the key to the program and all levels especially the local level, will need to be responsive to VPDs data. A strong surveillance system may determine which areas or population groups are most affected by VPDs and determines whether the programme is performing as expected or not.

There is substantial investment in vaccinating eligible population, in collecting VPD data; but without a commensurate investment in analyzing the data for planning and action- it is unlikely to yield significant returns. This manual will guide the programme in doing it efficiently.

I congratulate the Expanded Programme on Immunization for updating the surveillance manual together with various stakeholders, partners, national and international experts. I would like to take this opportunity to applaud the World Health Organization, Bangladesh for their overall technical assistance in updating and publishing the 4th edition of the manual. Finally, I convey my heartfelt thanks to all who are engaged in providing immunization services including surveillance to save the life of thousands of children from vaccine preventable diseases.

Professor Dr. Abul Basher Mohammad Khurshid Alam
Director General
Directorate General of Health Services
Mohakhali, Dhaka 1212

FOREWORD

Immunization is one of the most cost-effective public health interventions for protecting individuals and the public. The Expanded Programme on Immunization (EPI) is very successful in Bangladesh. The Government of Bangladesh envisages to protect all eligible beneficiaries from Vaccine Preventable Diseases (VPDs). For it, surveillance is fundamental to program planning and implementation and is a crucial factor for accelerating progress.

Surveillance activity in EPI for VPDs started in 1995 with case-based Acute Flaccid Paralysis (AFP) surveillance for Polio eradication. After that, some more diseases and issues have been incorporated for surveillance including Neonatal Tetanus (NT), Measles, Congenital Rubella Syndrome (CRS), Acute Encephalitis Syndrome (AES) with the goal to eliminate and control. Additionally, other VPDs under national EPI are reported on a weekly basis from all government health facilities and major private facilities.

The current edition of this surveillance manual is a product of extensive consultations of documents, inputs from different stakeholders, and reviewed by renowned experts. It highlights Bangladesh context and focuses some critical activities by indicators.

Effective surveillance is critical specially to determine which areas or population groups are most affected by VPDs, where vaccination and other relevant services are inadequate, so that resources can be targeted to the populations and areas most in need. Data on changes in VPD incidence and mortality are also needed to determine whether it is performing as expected or whether adjustments in the scale or blend of interventions are required.

I sincerely hope that managers at all levels and other personnel both in government and non-government organizations will responsively read this manual and will follow the guidelines in enhancing EPI and VPD surveillance in the country.

Dr. Mohammed Nizam Uddin
Director and Line Director, MNC&AH
DGHS, Mohakhali, Dhaka 1212

PREFACE

The Expanded Programme on Immunization (EPI) is one of the most successful programmes in Bangladesh, and surveillance is fundamental to its planning and implementation. Presently, the programme has been providing vaccine against 10 diseases by reaching the community through fixed and outreach sites and implementing facility and community-based surveillance for Vaccine Preventable Diseases (VPDs).

To guide the program in enhancing VPD surveillance, this manual was first developed in 1997 though the country started surveillance activity in EPI for VPDs in 1995 with Acute Flaccid Paralysis (AFP) surveillance for Polio eradication. This manual is for indicator-based surveillance with following key contents:

- Surveillance network
- Case definition
- Case investigation, sample collection, storage, and transportation for laboratory confirmation
- Public health measure for diseases with specific programmatic goal (i.e., eradication, elimination)

The manual is designed as a practical guide for health staff to implement surveillance activities at the central and peripheral levels. The primary target audiences for this manual are government health staffs and partners involved in the implementation of VPD surveillance and programmatic monitoring and evaluation (M&E). Moreover, the use of the manual will help in identifying areas and populations groups most affected by VPDs, setting up effective interventions and providing information about trend and distribution of VPD cases and deaths.

Precise epidemiological intelligence drives smart strategic decisions and helps in ensuring that the interventions are targeted and tailored to specific localities and populations. I sincerely hope that the EPI programme will get a good guidance through this manual to enhance VPD surveillance in the country, ultimately to protect all eligible beneficiaries from Vaccine Preventable Diseases.

I would like to convey my heartfelt thanks to all who are engaged in providing immunization services and saving the life of thousands of children from vaccine preventable diseases. I would like to take this opportunity to applaud the World Health Organization, Bangladesh for their technical assistance in updating and publishing this edition of the manual.

Dr. S M Abdullah Al Murad
Programme Manager
Expanded Programme on Immunization (EPI)
MNC&AH, DGHS, Mohakhali, Dhaka 1212

LIST OF CONTRIBUTORS

(Not according to the seniority)

DGHS

1.	Dr. Mohammed Nizam Uddin	Director & Line Director, MNC&AH

EPI HQ

1.	Dr. S M Abdullah Al Murad	Programme Manager, EPI, DGHS
2.	Dr. Jesmin Ara Khanam	Deputy Director-EPI, DGHS
3.	Dr. Md. Tofazzal Hossain	Assistant Director-EPI, DGHS
4.	Dr. Tanvir Hossen	DPM-EPI Surveillance, EPI DGHS
5.	Dr. Md. Monjurul Islam	DPM-Field Service, EPI DGHS
6.	Dr. Md. Firoz	DPM-IEC & BCC, EPI DGHS
7.	Dr. Rajib Sarkar	Medical Officer, EPI DGHS
8.	Ms. Kohinoor Begum	Training Officer, EPI DGHS

World Health Organization (WHO)

1.	Dr. Rajendra Bohara	Team Leader-IVD, WHO Bangladesh
2.	Dr. Md. Tanbirul Islam	NPO-EPI, IVD, WHO
3.	Dr. Chiranjit Das	NPO-Immunization, IVD, WHO
4.	Dr. Md. Ariful Islam	Senior National Consultant-Measles Elimination, IVD, WHO
5.	Dr. Pallab Chakraborty	Urban Immunization Focal Person, IVD, WHO
6.	Dr. Sheikh Md. Monirul Alam	NPO-Divisional Coordinator, IVD, WHO
7.	Dr. Imong Prue Chowdhury	NPO-Divisional Coordinator, IVD, WHO
8.	Dr. Md. Jahangir Alam	NPO-Divisional Coordinator, IVD, WHO
9.	Dr. Md. Arifur Rahman	NPO-Divisional Coordinator, IVD, WHO
10.	Dr. A K M Kamruzzaman	NPO-Divisional Coordinator, IVD, WHO
11.	Dr. Jobayer Al Mamun	NPO-Divisional Coordinator, IVD, WHO
12.	Md. Fozle Azim	Data management Team, IVD, WHO
13.	Md. Hasanuzzaman Khan	Data management Team, IVD, WHO

UNICEF

1.	Dr. Md. Shamsuzzaman	Consultant, UNICEF

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ACRONYMS

Acronym	Expanded Form
ADS	Auto-disable Syringe
AEFI	Adverse Events Following Immunization
AFP	Acute Flaccid Paralysis
CES	Coverage Evaluation Survey
CFR	Case Fatality Ratio
CIF	Case Investigation Form
CHO	Chief Health Officer (of City Corporation)
cMYP	Comprehensive Multi-Year Plan
CRI	Congenital rubella infection
CRS	Congenital Rubella Syndrome
CS	Civil Surgeon
EPI	Expanded Program on Immunization
GVAP	Global Vaccine Action Plan
HA	Health Assistant
HI	Health Inspector
HIV	Human Immunodeficiency Virus
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IHR	International Health Regulations
IMCI	Integrated Management of Childhood Illness
IPC	Interpersonal Communication
IPV	Inactivated Polio Vaccine
ITAG	Immunization Technical Advisory Group
JRF	Joint Reporting Form
MCV	Measles-containing vaccine
MCV1	Routine First Dose of Measles-containing Vaccine
MCV2	Routine Second Dose of Measles-containing Vaccine
MDG	Millennium Development Goal
MRCV	Measles-rubella-containing Vaccine
MR	Measles-rubella

Acronym	Expanded Form
MMR	Measles-mumps-rubella
MO	Medical Officer
NGO	Non-governmental Organization
NID	National Immunization Day
NTAGI	National Technical Advisory Group on Immunization
NVC	National Verification Committee for Measles, Rubella & CRS elimination
OPD	Outpatient Department
ORI	Outbreak response immunization
PCV	Pneumococcal Conjugate Vaccine
PHC	Primary Health Centre
RCV	Rubella Containing Vaccine
RI	Routine Immunization
RNA	Ribonucleic Acid
SAGE	Strategic Advisory Group of Experts
SEAR	South-East Asia Region of WHO
SIA	Supplementary Immunization Activities
SIMO	Surveillance & Immunization Medical Officer (SIMO)
SoP	Standard Operating Procedures
SSPE	Subacute Sclerosing Panencephalitis
VPD	Vaccine Preventable Disease

1. Introduction

1.1 Disease Surveillance: General Concept

Disease surveillance may be defined as ongoing collection *and analysis* of information about cases of a disease as a basis for *planning, implementing and evaluating* disease prevention and control activities. The type of information collected by disease surveillance consists of descriptive epidemiologic categories of **time** (date of symptom onset), **place** (where infected) and **person** (age, sex, vaccination status, mortality etc.).

Disease surveillance may be **active or passive.** Surveillance is **active** when a designated official collects data from individuals or registers, logbooks, medical records, etc. Surveillance is **passive** when data are sent from designated individuals or facilities.

Disease surveillance may be **facility-based or community-based.** Facility-based disease surveillance refers to the collection of data (actively or passively) from fixed sites. Community-based disease surveillance refers to collection of data from individuals in the community rather than from fixed facilities.

Disease surveillance data may be **aggregate or case based.** Aggregate disease surveillance reports represent sum of number of cases presented by one or more attributes (place, age group, vaccination status etc.). Case-based disease surveillance refers to collection and management of data of individual cases, usually using case investigation form for each case.

1.2 Objectives of Acute Flaccid Paralysis (AFP) and Vaccine Preventable Diseases (VPDs) Surveillance

The objectives of AFP and VPDs surveillance are to:

- Characterize epidemiology and measure burden of vaccine preventable diseases.
- Detect and investigate outbreak and take immediate actions for preventing additional cases or deaths during outbreaks of any vaccine preventable disease.
- Help public health officials at the upazila, district, municipality, city corporation, division and national level to develop more effective strategies to prevent diseases.
- Measure the impact of vaccination programme.
- Identify high risk population and areas.
- Identify problems in service delivery (e.g. sub-potent vaccine, adverse event).
- Measure the impact of specific health interventions and determine if a particular disease prevention strategy is effective (e.g. supplementary vaccination campaigns).

1.3 AFP and VPDs Surveillance System in Bangladesh

Expanded Programme on Immunization (EPI) is assigned for management of AFP and VPDs surveillance system in Bangladesh. The diseases under surveillance are Polio (any age), AFP (<15 years), AES (any age), Neonatal Tetanus (<28 days), Tetanus (any age after neonatal period), Measles (any age), CRS (Congenital Rubella Syndrome, any infant less than 1 year of age), Diphtheria (any age), Pertussis (any age) and Tuberculosis (< 5 years).

AFP and VPDs are reported from static health facilities on weekly basis using 'AFP and EPI Diseases Weekly Line Listing Form for Hospitals and Upazila Health Complexes' *(Annexure 02)*. Designated health facilities send weekly passive reports to Civil Surgeons/Chief Health Officers. Civil Surgeons and Chief Health Officers of all districts and City Corporations send the compilation of passive reports to the EPI HQ. If no cases of AFP and VPD are found, then report indicating "ZERO" is sent. Currently 792 health facilities are under passive surveillance.

In addition to passive reporting, weekly active surveillance is conducted for AFP, AES, Measles, Neonatal Tetanus and CRS in major hospitals. Currently 167 major hospitals are under active surveillance.

1.3.1 Disease Surveillance Focal Person (DSFP)

The local health official responsible for disease surveillance activities is called the Disease Surveillance Focal Person **(DSFP).** The DSFP is the Civil Surgeon (CS) for district, Chief Health officer (CHO) for City Corporation, Upazila Health & Family Planning Officer (UH&FPO) for Upazila and Municipal Medical Officer (MMO) for Municipality. If MMO post is lying vacant then UH&FPO of respective Upazila acts as DSFP for that municipality.

The **DSFP** is responsible for managing all disease surveillance activities in his/her assigned geographic area. The surveillance activities include:

- Monitoring and ensuring weekly passive surveillance for AFP, Measles/Rubella, CRS, Neonatal Tetanus, AES, Tetanus after neonatal period, Diphtheria, Pertussis, Tuberculosis under 5 years.
- Monitoring and ensuring weekly active surveillance for AFP, Measles/Rubella, CRS, Neonatal Tetanus and AES.
- Ensuring timely investigation of and response to AFP, Measles/Rubella, CRS, NT and AES cases and suspected outbreaks of Measles or other EPI disease, as and when required and as decided by the programme.
- Ensuring that all data from cases and outbreaks are properly collected, compiled, analyzed and interpreted for appropriate local action.
- Ensuring that data of passive surveillance, case investigation and outbreak investigation are forwarded timely to EPI HQ through proper channel.

1.3.2 Local Surveillance Officer (LSO)

To assist DSFP in carrying out his/her surveillance responsibilities. DSFP should designate Local Surveillance Officer (LSO) who would be specifically responsible for implementing surveillance activities including case investigation, outbreak investigation, outbreak/case response immunization and report to DSFP.

Table 1: List of DSFPs and LSOs

Location	DSFP	LSO
District	Civil Surgeon	Medical Officer-CS (MOCS)
City Corporation	Chief Health Officer	Health Officer/ Assistant Health Officers/ Zonal Medical Officer
Upazila	UH&FPO	MO-DC/ MO-MCH
Municipalities with medical officers	Municipal Medical Officer	Municipal Medical Officer
Other municipalities where MMO post vacant	Respective UH&FPO	MO-DC/ MO-MCH of UHC

1.3.3 Hospital Surveillance Officer (HSO)

To facilitate and coordinate passive reporting of AFP & VPD cases, carry out investigation and other surveillance activities in Hospitals, Hospital Surveillance Officer (HSO) should be designated by the Director/ Superintendent of the Hospital. HSO is responsible for managing surveillance system within the hospital and for preparing and submitting 'AFP and EPI Diseases Weekly Line Listing Form for Hospitals and Upazila Health Complexes' *(Annexure 02)* to DSFP. For case-based surveillance HSO is responsible for notification, initiate case investigation, ensure sample collection, storage and sending of specimen to the designated National Laboratory (specimens of AFP, suspected Measles, suspected/clinically confirmed CRS case to National Polio and Measles Laboratory (NPML) and specimens of AES case to Institute of Epidemiology, Disease Control and Research (IEDCR).

1.3.4 Surveillance and Immunization Medical Officer (SIMO)

WHO Bangladesh has assigned Surveillance & Immunization Medical Officer (SIMO) and Divisional Coordinators (NPO EPI DC) in district and division respectively to work in close collaboration with GoB counterpart to support surveillance activities at field level.

Surveillance & Immunization Medical Officers' (SIMOs) responsibilities:

- Provide technical assistance to local health authorities in coordinating AFP and VPDs surveillance activities.
- Provide technical assistance to ensure timeliness and completeness of reporting.
- Facilitate investigation and re-investigation (where applicable) of AFP and immediately reportable VPD cases that requires either laboratory confirmation or community level response or both activities.
- Provide necessary orientation to relevant personnel to establish/ strengthen surveillance network.
- Coordinate activities for timely collection and transportation of specimens.
- Provide technical assistance in case/outbreak response activities.
- Analysis and feedback of surveillance data.

SIMOs are primarily responsible for providing technical support, supervise and monitor entire process of surveillance.

1.3.5 Role of Hospital Physician

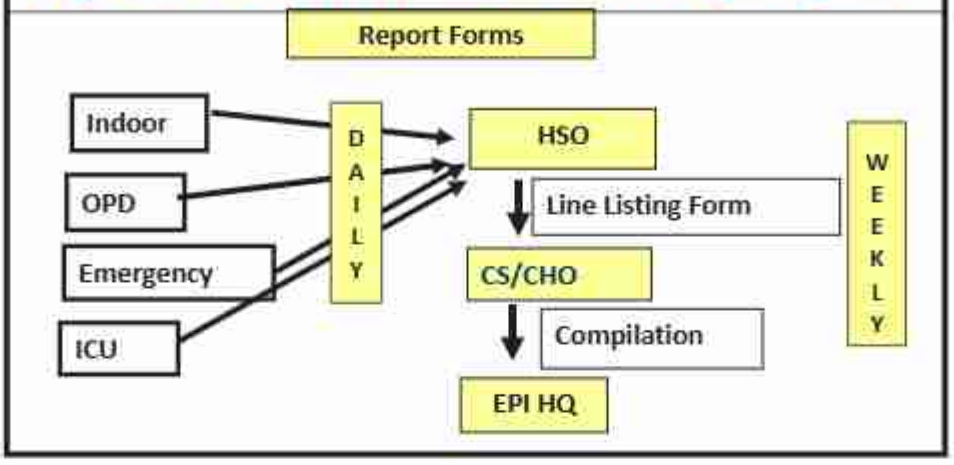
All physicians of facilities should immediately notify any suspected AFP, Measles, CRS, NT and AES cases to HSO and DSFP or SIMO. All suspected measles, CRS, NT and AES cases while visiting the hospitals are to be investigated by attending physicians. HSO should facilitate investigation and sample collection of AFP, , Measles, CRS and AES cases. All Diphtheria, Pertussis, Tetanus after neonatal period and Tuberculosis under 5 years to be reported to HSO by filling up the 'AFP & EPI Disease Report Form' on daily basis.

1.4 Passive surveillance of AFP and VPDs at health care facilities

- All cases of AFP and VPDs at the outpatient, emergency and inpatient department within health care facilities to be identified and notified.
- All AFP, Measles, CRS, AES and Neonatal Tetanus to be identified, notified and investigated.
- The clinicians (resident physicians, resident medical officers, machine specialist, pediatricians, neurologists, consultants, medical officers and others) of the health care facility need to collect information from the patients they attended and fill up the 'AFP & EPI Disease Report Form' *(Annexure 01)*.
- The 'AFP & EPI Disease Report Form' is to be submitted to Hospital Surveillance Officer (HSO) at the end of the day.
- The HSO will review the reporting forms to ensure that all reported AFP, Measles, CRS, NT, AES cases have been notified to DSFP or SIMO and properly investigated. S/he will prepare and send the 'AFP & EPI Disease Weekly Line Listing Form' to DSFP *(Annexure 02)*.
- Completed 'AFP & EPI Disease Weekly Line Listing Form' to be reached at DSFP level (Civil Surgeon/Chief Health Officer) of the district or city corporation by Tuesday of following epidemiologic week including "Zero Report".
- DSFP will compile the data of the line listing form of all the reporting units of his/her District/City Corporation in the 'AFP & EPI Diseases Weekly Compilation Form for Districts/City Corporations' *(Annexure 03)* and submit the report to EPI HQ. The report to be reached to EPI HQ by Tuesday of following epidemiologic week including "Zero Report".

Note: The list of epidemiological week (Sunday to Saturday) is available with AFP & EPI Disease Weekly Line Listing Form:

Figure. 1: AFP and VPD Passive Surveillance Reporting Flow



1.5 Weekly Active Surveillance of AFP, Measles, CRS and NT Cases in Facilities

- The LSO along with the SIMO will visit the assigned hospital every week to review inpatient, outpatient and emergency registers and other relevant documents (e.g. report books, medical records) for any suspected AFP, Measles, CRS, NT and AES case.
- S/he will contact clinicians (resident physicians, resident medical officers, machine specialist, pediatricians, neurologists, consultants, medical officers and others) and nurses to identify new cases of AFP, Measles, CRS, NT and AES detected in the previous week.
- The visit to be documented by signing the registers and other relevant documents that are checked.
- The LSO and/or SIMO will complete the 'AFP, Measles, CRS, NT and AES Weekly Active Surveillance Form' *(Annexure 04)* and submit the report, including "Zero Report" to EPI HQ that to be reached by Tuesday of following epidemiologic week.

1.5.1 Role of UH&FPO/MMO/ZMO/AHO

- Encourage reporting of all AFP and reportable cases of VPD under national EPI.
- Instruct field staff to identify any outbreak.
- Ensure line listing of cases and send the appropriately filled form to the Civil Surgeon/ Chief Health Officer (DSFP) which to be reached by next Tuesday including "Zero Report".
- Ensure investigation and filling up appropriate 'Case Investigation Form' (CIF) of identified suspected AFP, Measles, CRS, NT and AES case.
- Ensure specimen collection of all confirmed AFP, suspected Measles, CRS and AES cases and transportation to designated Laboratory with case investigation form.
- Ensure additional case searching in area of event, Case Response Immunization (CRI), Outbreak Response Immunization (ORI), Contact Tracing with appropriate response as applicable etc.

- Ensure analysis and interpretation of collected data of investigated cases for local action.
- Appropriate case management and follow up.
- Dissemination of information to District/City Corporation.

1.5.2 Role of Civil Surgeon/ Chief Health Officer

- Civil Surgeon/Chief Health Officer will monitor weekly line listing of cases submitted by health facilities.
- Ensure compilation of all weekly passive surveillance reports and submit to EPI HQ.
- Organize outbreak investigation through District/City Corporation Rapid Response Team (RRT).
- Ensure collected data are compiled, analyzed, interpreted and necessary actions have been taken at local level.
- Analyze disease patterns and trends and produce report.
- Monitor timeliness and completeness of weekly reporting.

1.5.3 Role of EPI Manager at National level

- Monitor surveillance performance using standard indicators.
- Provide technical support to national, division and district level activities.
- Supervise all level activities for surveillance of AFP and VPDs.
- Coordinate with the designated laboratory i.e. specimens of AFP, suspected Measles, suspected/clinically confirmed CRS case to National Polio and Measles Laboratory (NPML) and specimens of AES case to Institute of Epidemiology, Disease Control and Research (IEDCR).
- Analyze disease patterns and **trends**, interpret surveillance data in conjunction with the routine immunization coverage data and facilitate producing report.
- Provide feedback to all levels.
- Use surveillance data for programmatic measures and national level planning.

1.6 Role of Field Workers and Supervisors

All field workers of GoB, private sector and NGOs should identify and immediately notify any ***suspected AFP, Measles and CRS case to DSFP and suspected Neonatal Tetanus (NT) and any Neonatal Death (ND) cases to respective supervisors***. After verification, if the ND or suspected NT satisfies the operational case definition for Neonatal Tetanus, supervisor should report to DSFP immediately. Any suspected measles outbreak to be notified immediately to his/her supervisors or DSFP. All other suspected vaccine preventable diseases to be reported weekly to respective supervisors who will report to his/her manager.

1.7 Role of Health Care Providers and key informants in the community

All other health care providers (e.g. private practitioner, village doctors, traditional healers etc.) and potential informants (e.g. Imam, teacher, local leader etc.) to be encouraged to notify any suspected AFP, Measles, CRS, Neonatal Tetanus including Neonatal Death (ND) immediately to nearby health facility or field worker.

2. Poliomyelitis & AFP Surveillance

2.1 Introduction

Poliomyelitis is a highly infectious disease caused by poliovirus. The words polio (grey) and myelon (marrow, indicating the spinal cord) are derived from the Greek. It is the effect of poliomyelitis virus on the spinal cord. Michael Underwood first described a debility of the lower extremities in children that was recognizable as poliomyelitis in England in 1789. The first outbreaks in Europe were reported in the early 19th century.

Poliomyelitis

Highly infectious disease caused by polio virus.

First described by Michael Underwood in 1789.

The first outbreaks in Europe were reported in the early 19th century.

2.1.1 Causative agent

Poliomyelitis (polio) is a highly infectious disease caused by poliovirus. Poliovirus is a member of the enterovirus subgroup, family Picornaviridae. Enteroviruses are transient inhabitants of the gastrointestinal tract and are stable at acid pH. Polio Virus is a small virus with an RNA genome. There are 3 types of wild poliovirus (WPV) - types 1, 2 and 3. In September 2015, WPV type 2 was officially declared eradicated. Type 3 wild poliovirus was declared eradicated in October 2019. It was last detected in November 2012. WPV type 1 is the only wild poliovirus type that remains in circulation.

Poliovirus

Enterovirus (RNA)

Three serotypes: 1, 2, 3

Serotype 2, declared eradicated in September 2015

Serotype 3, declared eradicated in October 2019

Rapidly inactivated by heat, formaldehyde, chlorine and ultraviolet light.

The poliovirus is rapidly inactivated by heat, formaldehyde, chlorine and ultraviolet light.

Vaccine-associated paralytic polio (VAPP)

- Vaccine-associated paralytic polio (VAPP) OPV is made with live attenuated (weakened) polioviruses that can result in a case of vaccine-associated paralytic polio (VAPP) in approximately 1 in 2.7 million doses of OPV.
- VAPP is caused by a strain of poliovirus that has genetically changed in the intestine from the original attenuated vaccine strain contained in OPV.
- Following OPV administration, Poliovirus replicates within intestine. This replication is error prone and genetic change takes place at VP1 nucleotide position of virus genome.
- It is associated with a single dose of OPV administered in a child or can occur in a close unvaccinated or non-immune contact of the vaccine recipient who is excreting the mutated virus.

Vaccine-derived polioviruses (VDPVs)

The attenuated viruses in live OPV vaccines (Sabin viruses) may, through prolonged replication in an individual or in a community, re-acquire the neurovirulence and transmissibility characteristics of WPV. They may then become cVDPVs that cause isolated cases or outbreaks of paralytic

poliomyelitis. During 2011– 2015, almost 90% of reported cVDPV cases (204/230) were associated with the type 2 component of tOPV.

VDPVs are genetically divergent forms of the original Sabin vaccine virus conventionally defined by >1% genetic divergence (or >10 nucleotide [nt] changes) for PV1 and PV3 and >0.6% (or >6 nt changes) for PV2. These viruses are further subdivided into 3 categories:

(1) cVDPVs, when evidence of person-to-person transmission in the community exists;

(2) immunodeficiency-associated VDPVs (iVDPVs), which are isolated from some people with primary B-cell or combined immunodeficiency disorders (with defects in antibody production) who may have prolonged VDPV infections (in individual cases excretion has been reported to persist for 10 years or more;

(3) ambiguous VDPVs (aVDPVs), which are either clinical isolates from persons with no known immunodeficiency, or sewage isolates of unknown origin.

The term 'persistent cVDPV' refers to cVDPVs that continue to circulate for >6 months following detection. Persistent cVDPVs represent programmatic failures to contain the cVDPV outbreak within 6 months of detection.

2.1.2. Reservoir

Humans are the only reservoir of poliovirus, which is transmitted most frequently by persons with inapparent infections. There is no asymptomatic carrier state except in immune deficient persons.

2.1.3. Communicability

Poliovirus is highly communicable, with seroconversion rates among susceptible household contacts of children nearly 100%, and greater than 90% among susceptible household contacts of adults. Persons infected with poliovirus are most infectious from 7 to 10 days before and after the onset of symptoms.

2.1.4. Transmission

Person-to-person spread of poliovirus via the fecal-oral route is the most important route of transmission, although the oral-oral route is possible. Poliovirus multiplies in the intestines and is spread through the feces. The time between infection and onset of minor illness is 3-8 days; the time between infection and onset of paralysis is 10-21 days. The virus spreads rapidly to non-immune persons; transmission is usually widespread by the time of paralysis onset. The virus is intermittently excreted for up to 2 months or more after infection, with the heaviest excretion occurring just before paralysis and during the first two weeks (14 days) after paralysis onset.

Poliovirus infection typically reaches its peak in the summer months in temperate climates. There is no seasonal pattern in tropical climates.

2.2.1. Pathogenesis

The virus enters through the mouth, and primary multiplication of the virus occurs at the site of implantation in the pharynx and gastrointestinal tract. The virus is usually present in the throat and in the stool before the onset of illness. One week after onset there is less virus in the throat, but virus continues to be excreted in the stool for several weeks. The virus invades local lymphoid tissue, enters the bloodstream, and then may infect cells of the central nervous system. Replication of poliovirus in motor neurons of the anterior horn and brain stem results in cell destruction and causes the typical manifestations of poliomyelitis.

Pathogenesis

Entry into mouth

Replication in pharynx, GI tract

Hematologic spread to lymphatics and central nervous system

Viral spread along nerve fibers

Destruction of motor neurons

2.2.2. Clinical features

The incubation period for nonparalytic poliomyelitis is 3-6 days. For the onset of paralysis in paralytic poliomyelitis, the incubation period usually is 7 to 21 days[1]. The response to poliovirus infection is highly variable and has been categorized based on the severity of clinical presentation.

Polio Infection outcome

1. Inapparent or asymptomatic-72%
2. Abortive poliomyelitis-24%
3. Non-paralytic aseptic meningitis 1-5%
4. Paralytic poliomyelitis <1%
    a. Spinal
    b. Bulbar
    c. Bulbospinal

Inapparent or asymptomatic poliomyelitis: Up to 72% of all polio infections are inapparent or asymptomatic. Infected persons without symptoms shed virus in the stool and are able to transmit the virus to others.

Abortive poliomyelitis: Approximately 24% of polio infections in children consist of a minor, nonspecific illness without clinical or laboratory evidence of central nervous system invasion. This clinical presentation is known as abortive poliomyelitis and is characterized by complete recovery in less than a week. This is characterized by a low-grade fever and sore throat.

Non-paralytic aseptic meningitis: Symptoms of stiffness of the neck, back and/or legs usually following several days after a prodrome similar to that of minor illness, occurs in 1%–5% of polio infections. Increased or abnormal sensations can also occur. Typically, these symptoms last from 2 to 10 days, followed by complete recovery.

Paralytic poliomyelitis: Less than 1% of all poliovirus infections result in flaccid paralysis. Estimates of the ratio of inapparent to paralytic illness vary from 100:1 to 1,000:1 (usually 200:1). Paralytic symptoms generally begin 1 to 10 days after prodromal symptoms and progress for 2 to 3 days. Generally, no further paralysis occurs after the temperature returns to normal. The prodrome may be biphasic, especially in children, with initial minor symptoms separated by a 1 to 7day period from more major symptoms. Additional prodromal signs and symptoms can include a loss of superficial reflexes, initially increased deep tendon reflexes and severe muscle aches and spasms in the limbs or back.

The illness progresses to flaccid paralysis with diminished deep tendon reflexes, reaches a plateau without change for days to weeks and is usually asymmetrical.

Patients do not experience sensory losses or changes in cognition. Many people with paralytic poliomyelitis recover completely and in most, muscle function returns to some degree. Weakness or paralysis still present 12 months after onset is usually permanent.

Paralytic polio is classified into three types, depending on the level of involvement. Spinal polio is most common and accounts for 79% of paralytic cases. It is characterized by asymmetric paralysis that most often involves the legs. Bulbar polio accounted for 2% of cases and led to weakness of muscles innervated by cranial nerves. Bulbospinal polio accounted for 19% of cases and was a combination of bulbar and spinal paralysis.

2.2.3 Case Fatality

The death ratio for paralytic polio is generally 2%–5% in children and up to 15%–30% in adults (depending on age). It increases to 25%–75% with bulbar involvement.

2.2.4 Prevention

The only way to prevent poliomyelitis is to develop immunity against poliovirus. Protective immunity against poliovirus infection develops by either immunization or natural infection.

The development of effective vaccines to prevent paralytic polio was one of the major medical breakthroughs of the 20th century. There are six different vaccines to stop polio transmission:

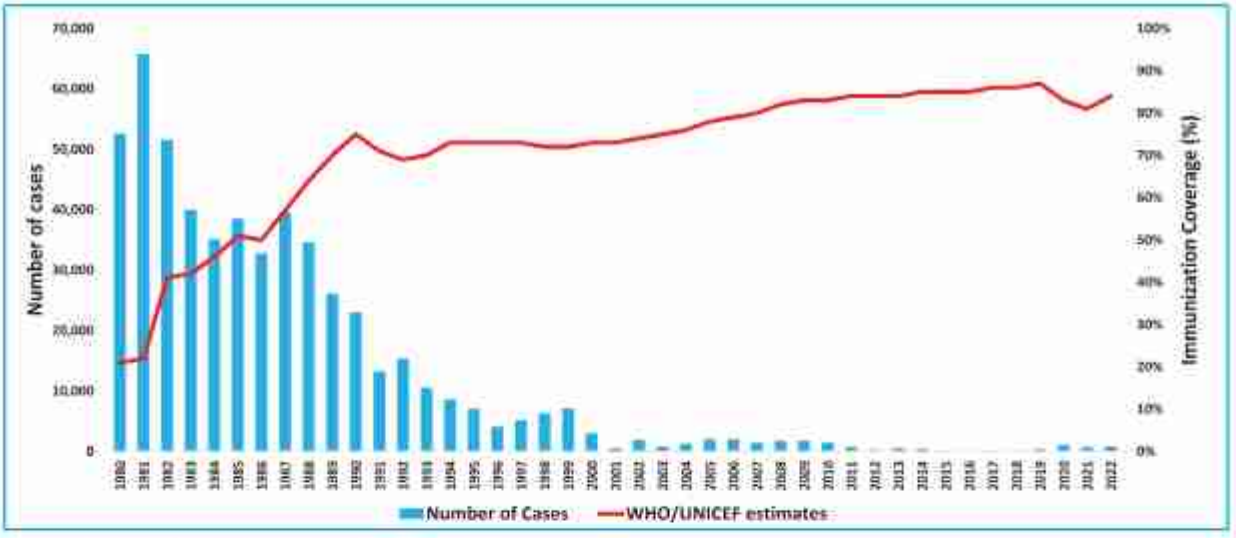
- Inactivated polio vaccine (IPV) – protects against poliovirus types 1, 2, and 3
- Trivalent oral polio vaccine (tOPV) – protects against poliovirus types 1, 2, and 3. tOPV is no longer in use since April 2016
- Bivalent oral polio vaccine (bOPV) – protects against poliovirus types 1, and 3
- Monovalent oral polio vaccines (mOPV1, mOPV2 and mOPV3) – protect against each individual type of poliovirus, respectively.
    - nOPV- To better address the evolving risk of type 2 circulating vaccine-derived poliovirus (cVDPV2), GPEI partners together with countries are deploying an innovative tool - novel oral polio vaccine type 2 (nOPV2). The vaccine is a modified version of the type 2 monovalent OPV (mOPV2), which clinical trials have shown provides comparable protection against poliovirus while being more genetically stable and less likely to be associated with the emergence of cVDPV2 in low immunity settings. This means that nOPV2 has the potential to be a significant tool to help stop outbreaks more sustainably.

If enough people in a community are immunized, the virus will be deprived of susceptible hosts and will die out. High levels of vaccination coverage must be maintained to stop transmission and prevent outbreaks occurring.

2.3 Poliomyelitis Surveillance

In 1988, when the WHO World Health Assembly (WHA) passed resolution WHA 41.28 calling for the global eradication of poliomyelitis (polio), the WHO South-East Asia (SEA) Region reported 25,711 paralytic polio cases, which accounted for more than 70% of the global polio case burden.

Figure2: Poliomyelitis Global annual reported cases and Pol3 coverage 1980-2022



Source: https://immunizationdata.who.int/

With intensive Global Polio Eradication Initiative (GPEI) efforts, including use of poliovirus vaccines through routine and intensive supplementary immunization as well as the rapid detection and response to poliovirus transmission, have led to a precipitous drop in the global incidence of poliomyelitis by > 99%. Moreover, the number of countries with endemic polio has reduced from 125 to just two in 2017 (Afghanistan and Pakistan). WPV types 2 and 3 were globally certified as eradicated in 2015 and 2019, respectively. Type 2 WPV, the last case was detected in Aligrah, Northern India in 1999; the last case of type 3 WPV was detected in northern Nigeria in 2012. Five out of six WHO regions are now free of WPV; the American Region in 1994, the Western Pacific Region in 2000, the European Region in 2002 and the African Region in 2020. The SEA Region steadily progressed to achieve the global goal of polio eradication and reported the last wild poliovirus (WPV) case from India on 13 January 2011 while the other ten member countries reported their last indigenous WPV cases on or before 2000. The Region was certified polio-free on 27 March 2014 and has remained polio-free since certification. While the Eastern Mediterranean Region remains with wild poliovirus circulation. Globally, only one wild serotype (poliovirus type 1) continues to be detected. Until poliovirus transmission is interrupted in these countries, all countries remain at risk of importation of polio, especially in the 'poliovirus importation belt' of countries from West Africa to the Horn of Africa.

2.3.1 Poliomyelitis surveillance in Bangladesh

Bangladesh was committed to eradicate poliomyelitis as a co-signatory of 1988 WHA resolution for global polio eradication. The countdown for polio eradication began in 1995, when Bangladesh showed leadership in the region by conducting its first National Immunization Days (NIDs) on March 16 and April 16, 1995. This historic event was supported by Rotary International, BASICS and USAID, SIDA, the Government of Japan, the US Centers for Disease Control and Prevention (CDC), UNICEF and the World Health Organization (WHO).

From 1995 to 2004, total twelve number of NIDs and one Sub-National Immunization Day (SNID) were conducted in Bangladesh. In 1999, total 29 Polio cases were reported from 18

districts in all 6 divisions. Before importation in 2006, last polio case detected in a slum area of Dhaka City Corporation on August 22, 2000. That was the last confirmed indigenous poliomyelitis case in Bangladesh before importation. Till then no Polio case was detected until early 2006 and Bangladesh was polio free for more than 5 years.

In January 2006 Polio importation with P1 serotype occurred in Bangladesh from neighboring state (Uttar Pradesh) of India. Rahima a 10 years old girl of Sadar Upazila of Chandpur District was the first Polio case; developed paralysis on 23 January 2006 and reported on 26 January 2006. Later, it was identified that Nesfatun, a 12-year girl of Panchbibi Upazila under Joypurhat district, though detected as second case, was virtually the first epidemiological victim of Polio; onset date 8 January 2006; since August 2000 when indigenous polio virus transmission was stopped.

Figure 3: Polio case reported in Bangladesh by year

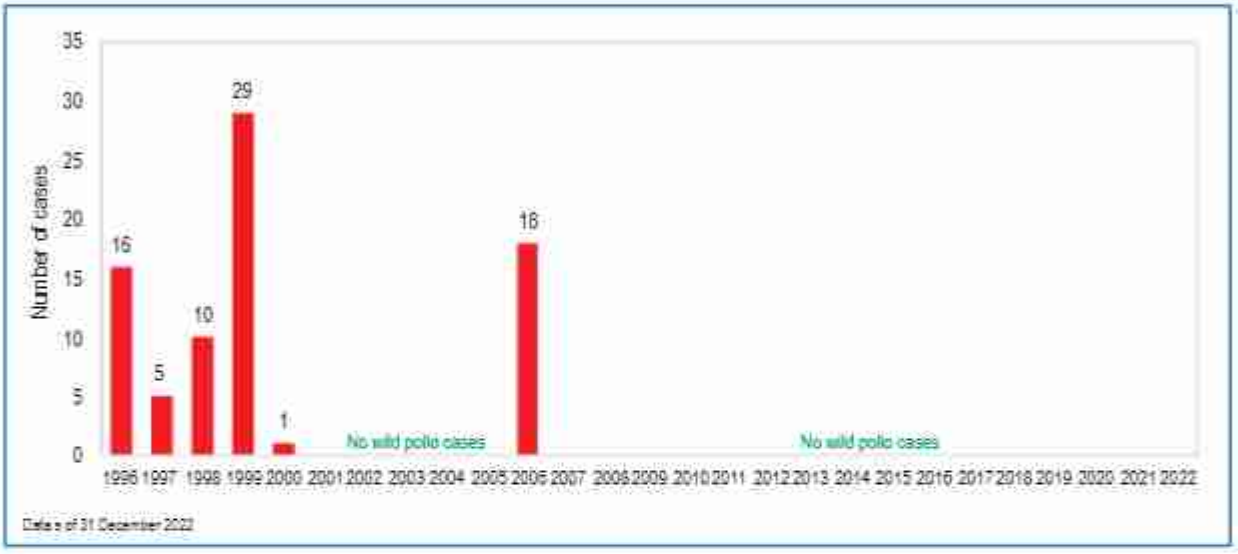


Figure 4: Polio outbreak in Bangladesh, 2006

After confirmation of Polio Virus circulation, Bangladesh organized unprecedented rapid response and provided opportunity to all children less than 5 years to receive mOPV with 4 rounds in 13th Special NIDs and another 2 rounds in 14th NIDs in 2006 with tOPV. On 22 November 2006 last polio case was identified in Chhatak, Sunamganj district. No polio case was identified after this case. A total of 18 Polio cases in 12 districts were identified after importation in 2006. Timely, aggressive responses with very high coverage in all 6 rounds of NIDs, strong routine EPI programme and special efforts to ensure "reaching the unreached" were the interventions for which Bangladesh was able to stop the virus circulation again.

2.3.2 Definitions related to polio eradication

Endemic: Uninterrupted circulation of indigenous strains of WPV within a country.

Introduction: Poliovirus introduced into an area that previously had no evidence of circulation, with genetic linkage to a country with endemic or outbreak transmission.

Re-established transmission: Following an introduction of WPV into a polio-free country, there is clear evidence of continued local circulation for more than 12 months.

Emergence: Detection of a genomically distinct strain of VDPV.

2.3.3 Strategies of Polio Eradication

- Strong Routine Immunization Programme
- National or Sub-National Immunization Days (NIDs/ SNIDs)
- Acute Flaccid Paralysis (AFP) Surveillance
- Mopping-up immunization

2.4 AFP Surveillance

Acute Flaccid Paralysis surveillance is very important element of Polio Eradication Program. The objectives of the AFP surveillance are to detect circulation of wild polioviruses or to demonstrate absence of wild polioviruses in presence of adequate level of surveillance. High level of AFP surveillance is important especially at the end stage of polio eradication initiative to allow the country to detect any importation of poliovirus from areas of endemic circulation, for mounting rapid, adequate, aggressive responses for controlling the resultant outbreak. Countries need to maintain certain standards of surveillance after cessation of wild poliovirus transmission to meet the stringent requirements to be certified as polio-free.

2.4.1 Suspected case definition for case finding

Nationwide AFP surveillance is the gold standard for detecting cases of polio, using the following recommended standard case definition:

A suspected case is any case presenting with AFP.

An AFP case is defined as a child <15 years of age presenting with recent or sudden onset of floppy paralysis or muscle weakness due to any cause (including Guillain-Barré syndrome), or any person of any age with paralytic illness if poliomyelitis is suspected by a clinician (paralysis is not present since birth or not a result of an injury).

A=Acute (Rapid progression from weakness to paralysis)

F=Flaccid (Loss of muscle tone, "floppy" as opposed to spastic or rigid)

P=Paralysis (Inability to move the affected part/weakness/loss of voluntary movement)

2.4.2 key steps of surveillance

- Finding and reporting AFP cases among children less than 15 years
- Collecting and transporting stool samples for analysis
- Isolating and identifying poliovirus in the laboratory and
- Classifying AFP cases.

2.4.3 Differential Diagnosis of AFP

The most common differential diagnosis of acute flaccid paralysis includes paralytic poliomyelitis, Guillain-Barré syndrome, Transverse myelitis and Traumatic neuritis. These diseases always presented with AFP.

Acute meningitides, Acute Encephalitis, Tumors, Epidural abscess, Spinal cord compression, Neuropathy of diphtheria, Clostridium botulinum (C. botulinum) toxin neuropathy, Tick bite paralysis, Myasthenia gravis, Osteomyelitis, Viral myositis, Hypokalemic periodic paralysis, post infectious polyneuropathy sometimes may present with Acute Flaccid Paralysis.

Distinguishing characteristics of paralytic polio are asymmetric, flaccid paralysis, fever and muscular pain at onset, rapid progression from weakness to paralysis, intact sensory nerve function and residual paralysis or weakness after 60 days.

Figure 5: Differential diagnosis of Acute Flaccid paralysis (AFP)

2.4.4 Case detection, notification and reporting

All health facilities and private practitioners should admit cases of AFP (both polio and non-polio) to the hospital and immediately report the case to the Disease Surveillance Focal Person (DSFP) in their area. The DSFP will send the Local Surveillance Officer (LSO) to investigate the case within 48 hours of notification and take appropriate actions. The SIMO also have to investigate/ reinvestigate every case in ensuring accuracy of case and quality of data. If the case is a resident of or travel to (within 30 days before or after onset of paralysis) different upazila, municipality or city corporation the local DSFP should notify the corresponding DSFP to conduct additional case finding and outbreak response immunization and to perform a 60+ day follow up examination of the case, if required.

Under reporting/silent areas need special activities

- Strengthen community surveillance
- Active case search
- Retrospective record review of different facilities
- Refresher training programme for different stakeholders

Active surveillance: is based on designated surveillance officers visiting the health facilities to search for and investigate unreported AFP cases through a retrospective review of health facility records, interviews with health workers and/or visit to wards to review cases. Surveillance sites should be prioritized according to their probability of seeing AFP cases i.e. those sites which have a higher probability of seeing an AFP case *(like district health facilities, tertiary health facilities, specialized institutions, major private health facilities, busy practitioners etc.)* should be visited more regularly *(i.e. active sites at least once in each epidemiologic week and passive sites fortnightly or monthly)*. Every surveillance officer should have a list of surveillance sites and a schedule of how these sites are visited. Each surveillance visit should be documented in patients register.

Passive surveillance: when data/reports are sent weekly by designated health facilities or individuals on their own, as a routine. Weekly reports are sent even if there were no cases of AFP detected (i.e. zero reports).

Community surveillance: where pharmacists, traditional healers, religious leader or community leaders may serve as a source of information on paralyzed children.

Important note

Operational target of a non-polio AFP rate at least 2/100 000 children less than 15 years.

During a polio outbreak and 12 months past after the most recent virus was isolated, non-polio AFP rates of 3/100 000 children less than 15 years are to be achieved in all districts.

2.4.5 Special efforts for underreporting /silent areas

Active case search

To find cases, health officials should contact key persons, such as community leaders, schoolteachers, day care center directors, social workers, leaders of women's organizations, mothers, traditional healers and religious leaders to inquire about recently paralyzed children in the community. Active case finding should be done in districts silent for one or more years and in high-risk population and areas for any children below 15 years who have had the **onset of AFP within the preceding 6 months**. All cases found to be immediately investigated *(≤48 hours of reporting)* and **two stool specimens** *(≥24 hours apart)* to be collected from cases with **paralysis onset within the last 3 months**.

Retrospective record review

Retrospective record reviews should be conducted for a minimum one-year period in different facilities (active and passive surveillance facilities) and rehabilitation centers to identify all patients under 15 years for any sign of AFP. If any case found, a standard case investigation form and summary of relevant clinical findings should be completed with follow up examination to present to the expert review committee for final classification.

Specific objectives for record review:

- To identify missed AFP cases.
- To determine the sensitivity of the AFP/polio surveillance system.
- To identify factors contributing to inadequate AFP surveillance.
- To raise awareness as to the importance of AFP surveillance through the involvement of key local personnel.
- To make recommendations on improved AFP surveillance policies and procedures.

2.4.6 Case Investigation

The DSFP and LSO will investigate the case by using case investigation form *(Annexure 05)* after receiving notification. The following steps should be followed.

Step 1: Assign a case identification number (ID) to the AFP case

ID Number is unique also called EPID number which include a three-letter country code (BAN) followed by 4 series of digits; district code (2 digit) where the case developed paralysis, upazila/municipal/CC code (3 digit code of Upazila/Municipality/CC where the case developed paralysis), the year of paralysis onset (2 digit) and the AFP case serial number for that place during that year (3 digit).

Example: AFP BAN - ## - ### - ## - ###

AFP BAN - 16 - 147 - 21 - 007

AFP (Reporting Case), BAN (country code), 16 (district code for Dhaka), 147 (upazila/cc code of Dhaka CC), 21 (year of onset of paralysis) and 007 (serial number of the AFP case in 2021)

If any AFP case travels and stays 30 days or more, prior to onset of paralysis in a place, that place should be considered as the address of case. And case ID to be assign accordingly.

Step 2: Mobilize all members of the investigation team and prepare for the investigation; contact SIMO by phone or via Civil Surgeons' office or through Municipal Medical Officer or Chief Health Officers office

As soon as the DSFP receives the notification of a suspected AFP case he should immediately contact to LSO and SIMO. The LSO actively participates in every AFP case investigation. LSO should bring the following materials with him to the field or hospital:

- Suspected AFP line listing form *(Annexure 20)*
- Investigation Form for Acute Flaccid Paralysis (AFP)
- Two stool specimen collection kits
- A stool transport carrier (a vaccine carrier specified for stool specimen collection and transportation) with 4 fully frozen icepacks.

SIMO will immediately meet DSFP and LSO and actively participate in AFP case investigation/reinvestigation.

Step 3: Investigate the suspected AFP case within 48 hours of report and fill up the Acute Flaccid Paralysis (AFP) Case Investigation Form *(Annexure 05)*

LSO should investigate the suspected AFP case within 48 hours after the report received by DSFP. If LSO is not available DSFP should designate any other trained Medical Officer to investigate the case or investigate the case him/herself. If SIMO is available LSO should proceed with him, otherwise LSO should proceed immediately without waiting for the SIMO to turn up. In such case SIMO should reinvestigate the case as soon as possible. The investigating team must go to the hospital or localities where the case is located. The investigator should carefully take the history and conduct physical examination of the case. The investigator should verify whether the case meets the criteria of AFP case and accordingly he/she will classify the case as **confirmed AFP** or **discarded as non-AFP**.

Important note

If any AFP case reported after 3 months of onset, the case investigation should be done but no stool collection is indicated. After 6 months of onset of paralysis no need to investigate the case but local effort should be taken to strengthen surveillance with this evidence of surveillance failure

For the confirmed AFP case the investigator should complete the Investigation form. If the case is in the community, he/she should be brought to UHC or any other health facility (for better management and quality stool samples collection).

If there is any possibility of not getting 2 adequate stools (e.g. respiratory distress may lead to death, delayed notification) SIMO/LSO should also fill up the additional information form and should collect the medical documents of this episode of illness.

*If any AFP case reported **after 3 months of onset**, the case investigation should be done but **no stool collection is indicated including contact sample collection**. After 6 months of onset of paralysis **no need to investigate the case** but local effort should be taken to strengthen surveillance with this **evidence of surveillance failure**.*

Step 4: Collect two stool specimens and send to the National Polio and Measles Laboratory (NPML) at the Institute of Public health (IPH) in Dhaka together with filled up Investigation Form for Acute Flaccid Paralysis

Stool specimens should be collected at the health facilities but if needed can be collected from the residence. All possible effort should be made to collect two **adequate** stool specimens within 14 days of onset of paralysis which is the most important indicator of AFP surveillance.

Adequate stool means that 2 stool specimens are collected at least 24 hours apart and within 14 days of paralysis onset and fulfill all the following criteria:

- Stool specimens are sufficient in amount (at least 8 grams- *half of the adult thumb size)*
- Stool specimens are preserved and transported maintaining cold chain (temperature between +2° to +8° Celsius)
- Stool specimens are not dried out on arrival at the national polio lab
- There is no evidence of leakage from the containers with stool specimens and
- Both stool specimens arrive at national polio lab within 72 hours of collection.

It is critical that stool specimens be kept cold (between +2° to +8° Celsius) after collection so that virus does not die.

The stool specimens' carrier should be separated and labeled; it should be used exclusively for specimen's transportation. The vaccine carrier and ice packs should be cleaned properly before and after use and should be kept aloof.

Simple enema/suppository can be used for constipated patients to collect stool specimens. In case of diarrhoea, stool specimens should be three fourth of the stool collection kits.

Hospital officials should help in investigating and collecting stool specimens as soon as possible from every reported AFP case. AFP case should be kept in the hospital until collection of 2 stool sample.

AFP stool collection kit with shipment carrier

Step 5: Record the required information in the AFP Line Listing Form *(Annexure 02)*

The information should be recorded in AFP line list to be prepared and displayed in the DSFP's office; it should be updated with laboratory stool report and follow-up (if indicated) report. LSO should ensure the line listing and its update. A soft copy of the line-listing form should be maintained at the offices of the UH&FPO /CHO and Civil Surgeon.

Step 6: Search for additional cases which may have occurred during the previous 6 months and conduct Outbreak Response Immunization (ORI) near the site where the case was believed to have been infected

Active searching should be conducted to identify any additional AFP case with the onset of paralysis within the last 6 months. Additional case finding should be ensured as soon as possible in the surrounding area of the residence of any AFP case/ or traveled area of any AFP case.

Outbreak Response Immunization (ORI) to be conducted for all AFP case after collection of stool. ORI to be done as quickly as possible after stool sample collection; the sooner it is done the better will be the result. At least 200 children under 5 years of age to be vaccinated *(single dose i.e., 2 drops of OPV)* irrespective of previous vaccination status. ORI need to be conducted in the area where the confirmed AFP case traveled to within the period of one month before and after the onset of paralysis. In general, OPV should not be given to the AFP case before the collection of stool specimens because of the potential for contamination of stool specimens with vaccine virus. However, OPV may be given if the 2 stool specimens have already been collected and the guardian or family insists. DSFP should ensure Outbreak Response Immunization.

Step 7: For cases without adequate stool sample, or cases with stool report of polio or vaccine derived or vaccine virus, conduct follow-up examination 60-90 days after paralysis onset and submit completed 60+ Day Follow Up Examination Form *(Annexure 06)* to EPI Headquarter

Sixty-day follow-up is done between the 60th and 90th day in certain categories of AFP cases to determine the presence/absence of residual paralysis. The presence of residual paralysis at this time is further evidence that the cause of paralysis is likely to be due to poliovirus. The 60+ days follow-up should not be done before the 60th day of onset of paralysis as there is still a possibility for the paralysis to resolve, resulting in "false positive" examination outcomes.

The following categories of AFP cases should undergo 60-day follow-up:

- AFP cases with inadequate stool specimen
- AFP cases with isolation of WPV/VDPV
- AFP cases with isolation of vaccine-type (Sabin-type) poliovirus.

During the 60-day follow-up examination, the investigator must:

- Verify with the family the developments since the first investigation and that all the information on the case investigation form is complete and correct.
- Clinically assess the child.
- Complete the 60+ days follow-up form *(Annexure 06)* and send it to EPI HQ soon after the follow-up is done. SIMO and DSFP will ensure the entre process.

Important note

Lost to follow up case: 3 attempts should be made to find out the case with proper documentation.

If patient changes address: DSFP should be notified on time.

If the case is lost to follow up at least 3 attempts to be made to find out and investigate the case. Each attempt to be documented filling out 60+ days follow up form in. If the case changes the address permanently or temporarily then the DSFP of that area should be informed by local DSFP to carry out 60+ day follow-up.

Step 8: For cases without adequate stool sample and 60+ days follow-up with residual paralysis or follow-up not done due to death or lost to follow-up – additional information form along with all medical records to be sent to EPI HQ for Expert Review Committee (ERC) to classify the case

If the stool sample are not 'adequate' and weakness or paralysis persists after 60+ days or the case died or lost to follow-up, the additional information and all medical records of the case

to be collected as soon as possible using Epidemiological and Clinical Investigation of the Case *(Annexure 07), photograph and short video-clip* and to be sent to EPI HQ along with 60+ days follow-up report. LSO with technical assistance from SIMO should ensure the documents.

2.4.7 Hot Case

EPI introduced the concept of 'Hot Case' in July 2004 to alert on the system at all levels on possibility of polio transmission.

Hot Case is any AFP case with any one of the following:

- History of travel to a country with polio circulation within a month of onset of AFP
- History of fever at onset of paralysis + asymmetrical proximal paralysis or patchy (inconsistent) paralysis with intact sensation
- Rapidly progressive paralysis leading to bulbar involvement and death
- Any case where qualified clinician/SMO suspects polio.

If any Hot case is identified, then an active case search should be launched to identify additional AFP cases as soon as possible. Hot case should be flagged to draw attention of national surveillance personnel and NPML. Stool test should be done within the shortest period of time and report to be traced for further intervention.

2.4.8 AFP case cluster

Two or more AFP cases in an union/urban ward in CC reported over a period of 4 weeks

and/or

Two or more compatible cases either in a single Upazila or 2 (two) neighboring Upazila or CC in 4 weeks period

Any one of the above situations warrant prompt investigation, reporting and documentation, to be sent to EPI headquarter, required for further programmatic measures those includes:

1. Assessment of population immunity of the area:
   - 1.1 OPV 3 coverage of last 3 years
   - 1.2 IPV 2 coverage of last 3 years
   - 1.3 Rapid Convenient Assessment (RCA) for ## OPV and IPV among children less than 5 years of age of each ward/s
2. Spot map of AFP cases that have occurred in the previous 2 years of the adjacent unions/urban wards *(even the adjacent unions/urban wards is in another upazila/district/Municipality/Zone)*
3. Reinforcement of surveillance network of the area

2.4.9 Inadequate stool and contact sample

If two stool specimens cannot be collected from the AFP case within 14 days of paralysis onset, or stool specimens arrive at a WHO-accredited laboratory in poor condition, one stool specimen each to be collected from five close contacts of index case preferably aged <5 years old but not beyond 15 years of age. Specimen should be collected from close family members

or household contacts, and if not possible, then from neighbors or playmates. The samples to be collected, stored and transported to NPML maintaining reverse cold chain with properly filled "laboratory request form for contacts' samples" *(Annexure 08)*. Contact sampling is to increase the sensitivity of detection of wild poliovirus transmission. Contacts' samples of index case to be collected up to 3 months of paralysis onset. Procedure of stool specimen collection, storage and transportation remains same as for AFP cases. A predesigned contact stool specimen form to be used.

2.4.10 Classification of AFP cases

Final classification of AFP cases includes three possibilities:

1. Confirmed Polio
2. Non-Polio AFP (Discarded polio case) and
3. Case compatible with Polio

Confirmed Polio

An AFP case is "confirmed" as polio only by the isolation of WPV or VDPV from any stool specimen. VDPVs are further classified as immunodeficient, circulating and ambiguous VDPVs. The isolation of the virus can be from the patient or from contacts.

Non-polio AFP (Discarded polio case) is an AFP case with no WPV or VDPV isolated from any of the two stool samples by national polio lab or any WHO reference laboratory on poliomyelitis and fulfills any of the following criteria:

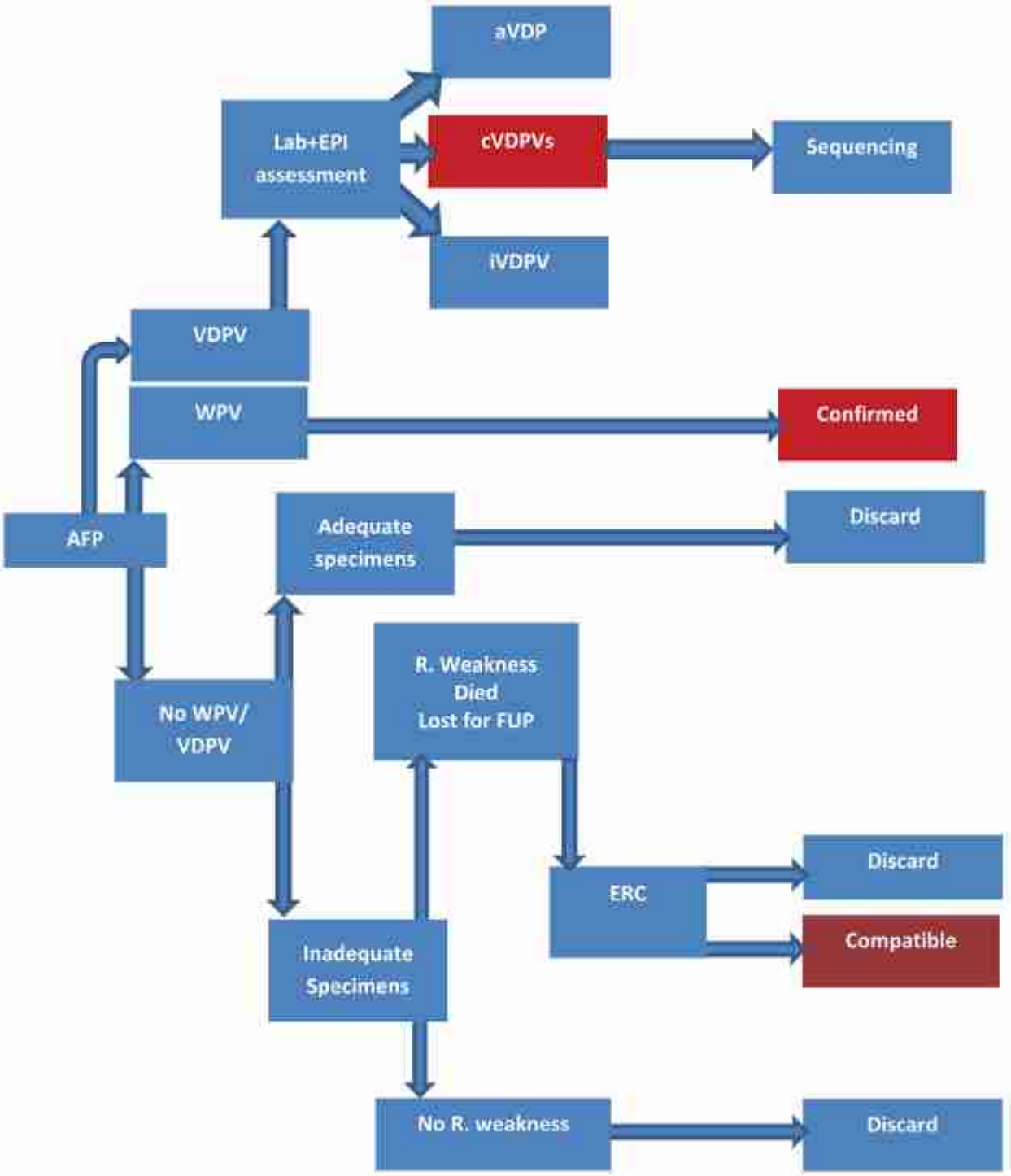
- the two specimens collected were adequate; or
- adequate stools could not be collected, but there was no residual paralysis during the 60+ days follow-up investigation; or
- adequate stools could not be collected, there was residual paralysis at 60+ days follow-up investigation, or 60+ follow-up investigation could not be done (either due to death or loss to follow-up); but after reviewing history, clinical features and necessary investigation reports, if the National Expert Review Committee (ERC) is convinced that this case is not compatible with polio.

Compatible with Polio:

If stool specimens are inadequate, final classification of the AFP case as either non-polio AFP or compatible with polio will depend on the results of 60+ days follow-up examination. If the 60+ days follow-up examination shows no residual weakness, the case is classified as non-polio AFP. If the AFP case has residual paralysis or 60+ days follow-up investigation could not be done either due to death or lost to follow-up, must be reviewed, and classified by the ERC. The AFP case might still be discarded as non-polio AFP, if the ERC has ruled out acute polio based on clinical and paraclinical findings. If that is not possible the ERC will do a final classification as polio compatible.

Polio-compatible cases are indicative of a failure of surveillance and serve as a reminder that all efforts must be made to ensure that cases are reported early enough to enable collection of adequate stool specimens from every AFP case.

Figure 6: Case classification scheme of AFP cases



2.4.11 Expert review committee

AFP cases are classified according to virological scheme *(figure 6)*. If the case has inadequate stool samples and 60 days follow up investigation showed residual paralysis, death, and lost for follow up, the case will be classified by a national Expert Review Committee (ERC). The ERC may request more clinical background and hospital documents and might examine the case to classify it as either compatible or discarded.

2.4.12 Public health intervention and response nOPV)

In May 2014 and in November 2015 in conjunction with the WHA, the WHO Director General declared the ongoing spread of polioviruses – WPV and cVDPV – to be a 'public health emergency of international concern'. In response, the Emergency Committee (EC) for polio, convened under the International Health Regulations (IHR), included cVDPVs in their remit for monitoring action and progress. All instances of WPV isolation in a previously polio-free country, VDPV2 anywhere in the world, and (related to the 2016 switch) all Sabin-like 2 viruses – must be reported immediately by the national authority (country) to WHO, regardless of type of isolate or its source (clinical case, environmental sample, other). Once WPV is identified in an area (district), appropriate and timely response should follow the same as for a positive case, including: rapid and thorough investigation of the cases, strengthening of AFP surveillance in the area, and implementing immediate and appropriate immunization activities.

Actions in Polio outbreak setting

Five pillars

1. Engagement of national government
2. Rapid risk assessment
3. Immunization response
4. Communication
5. Enhanced surveillance

Five strategic pillars are needed to effectively interrupt transmission in an outbreak setting: (i) a fully engaged national government, (ii) a rapid risk assessment and identification of transmission risk zones, (iii) a robust immunization response, (iv) effective communication and social mobilization, and (v) enhanced surveillance.

For further polio outbreak response requirements refer to the standard operation procedures (SOP) on responding to a poliovirus event or outbreak – general SOPs and protocol for poliovirus type 2.

2.5 Data management

The surveillance data should be reviewed on a weekly basis at the national and relevant subnational levels to detect and quantify disease occurrence, assess changing disease patterns over time, determine risks for disease, monitor the progress of the polio eradication programme and evaluate the performance of the AFP surveillance system itself. Analysis of AFP surveillance data is required for measuring the sensitivity and consistency of the surveillance system to ensure that it is functioning at the desired level.

AFP Surveillance Performance Indicators

Twelve performance indicators have been developed to measure the quality of AFP surveillance out of which ten are most important (shown in the table below). The indicators are helpful in identifying and correcting specific problems in the surveillance network.

Table 2: AFP Surveillance Performance Indicators

	Indicator	Target
1	Annual Non-Polio AFP rate in children <15 years old	≥2/100,000
2	Completeness of passive reporting from facilities	≥90%
3	Timeliness of passive reporting from facilities	≥80%
4	Suspected AFP cases investigated within 48 hours of notification	≥80%
5	Confirmed AFP cases with 2 stool specimens collected within 14 days after paralysis onset	≥80%
6	Stool specimens arriving at laboratory within 3 days after collection	≥80%
7	Stool specimens arriving at laboratory in "good" condition "good" = 1. Presence of un-melted ice or temperature <8^{0}C 2. Adequate volume (8 grams) 3. No evidence of leakage 4. No evidence of desiccation (drying)	≥90%
8	60+ follow up rate (Percentage of AFP cases with a follow-up investigation at least 60 days after onset of paralysis of a AFP cases with inadequate stool sample and AFP cases with positive isolates)	≥80%
9	Stool specimens with laboratory results within 14 days after specimen receipt	≥80%
10	Stool specimens from which non-polio enterovirus (NPEV) was isolated	≥10%

1. Surveillance Attribute: AFP rate

Indicator: Non-polio AFP rate per 100,000 <15 years children

Target: ≥2/100,000

Calculation:

$$\frac{\text{Number of reported non-polio AFP cases <15 years of age}}{\text{Total number of children <15 years of age}} \times 100{,}000$$

2. Surveillance Attribute: Timeliness of AFP reporting

Indicator: Reporting of AFP cases within 10 days of paralysis onset

Target: ≥80%

Calculation:

$$\frac{\text{AFP case reported within 10 days of paralysis onset}}{\text{Total number of reported AFP cases}} \times 100$$

3. **Surveillance Attribute:** Timeliness of case investigation

Indicator: AFP cases investigated within 48 hours of being reported

Target: ≥80%

Calculation:

$$\frac{\text{Number of case investigated} \leq 48 \text{ hours of being reported}}{\text{Total number of reported AFP cases}} \times 100$$

4. **Surveillance Attribute:** Adequate specimen collection

Indicator: Proportion of AFP cases with adequate stool specimens

Target: ≥80%

Calculation:

$$\frac{\text{AFP cases with 2 stool specimens collected within 14 days of onset of paralysis}}{\text{Total number of reported AFP cases}} \times 100$$

5. **Surveillance Attribute:** Duration of sample reaching

Indicator: Stool specimens reaching to laboratory within 72 hours of being collected

Target: ≥80%

Calculation:

$$\frac{\text{Total number of stool specimens arriving at national laboratory within 72 hours (3 days) of being collected}}{\text{Total number of stool specimens arriving at the laboratory}} \times 100$$

6. **Surveillance Attribute:** Condition of sample

Indicator: Stool specimens arriving at laboratory in "good" condition

Target: ≥90%

Calculation:

$$\frac{\text{Total number of stool specimens arriving at national laboratory in good condition}}{\text{Total number of stool specimens arriving at the laboratory}} \times 100$$

7. **Surveillance Attribute:** 60+ days follow up

Indicator: Percentage of AFP cases with a 60+ days follow-up investigation

Target: ≥80%

Calculation:

$$\frac{\text{Total number of cases with 60+ days investigation}}{\text{Total number of cases need 60+ days follow up}} \times 100$$

8. **Surveillance Attribute:** Timeliness of laboratory result

Indicator: Proportion of stool specimens with laboratory results within 14 days after specimen receipt

Target: ≥80%

Calculation:

$$\frac{\text{Total number of stool specimens with result within 14 days}}{\text{Total number of stool specimens arriving at the laboratory}} \times 100$$

9. **Surveillance Attribute:** NPEV isolated from specimens

Indicator: Proportion of Stool specimens with non-polio enterovirus (NPEV)

Target: ≥10%

Calculation:

$$\frac{\text{Total number of stool specimens from which NPEV is isolated}}{\text{Total number of stool specimens arriving at the laboratory}} \times 100$$

10. **Surveillance Attribute:** Completeness of passive surveillance

Indicator: Proportion of completeness of passive reporting

Target: ≥90%

Calculation:

$$\frac{\text{Total number of completed passive surveillance report}}{\text{Total number of report to be expected}} \times 100$$

11. **Surveillance Attribute:** Timeliness of passive surveillance

Indicator: Proportion of passive surveillance report received in time

Target: ≥80%

Calculation:

$$\frac{\text{Total number of passive surveillance report received in time}}{\text{Total number of report to be expected}} \times 100$$

12. **Surveillance Attribute:** Timeliness of active surveillance

Indicator: Proportion of active surveillance report received in time

Target: ≥80%

Calculation:

$$\frac{\text{Total number of active surveillance report received in time}}{\text{Total number of report to be expected}} \times 100$$

Special Considerations for polio Surveillance

Enterovirus surveillance

As polio-free status has been certified and it is challenging to maintain robust AFP surveillance, long-standing laboratory surveillance for enteroviruses provides a supplementary source of surveillance data on polioviruses.

Humanitarian emergencies

In humanitarian emergencies, rapid syndromic surveillance that is established should include AFP.

2.6 Environmental surveillance

Acute flaccid paralysis (AFP) surveillance is the gold standard for surveillance in the polio eradication initiative where stool specimens from individual AFP cases are tested for polioviruses. The examination of composite human fecal samples through environmental surveillance links poliovirus isolates from unknown individuals to populations served by the wastewater system. Environmental surveillance can provide valuable supplementary information, particularly in urban populations where AFP surveillance is absent or questionable, persistent virus circulation is suspected, or frequent virus re-introduction is perceived. In several countries, wild polioviruses have been detected in the environment in the absence of reported AFP cases. Environmental surveillance is also a potential tool for monitoring circulating vaccine-derived poliovirus (cVDPV) and assessing population immunity of populations vaccinated with inactivated polio virus (IPV). Therefore, environmental surveillance, or testing of sewage samples for poliovirus, can supplement AFP surveillance in some settings. The purpose of environmental surveillance is to identify poliovirus transmission that might occur in the absence of detected AFP cases, since <1% of new infections with WPV or VDPV leads to paralysis. Environmental surveillance can also be employed as part of a polio outbreak investigation if it is feasible to establish quality environmental surveillance.

12.6.1 Rationale of Environmental surveillance in Bangladesh

Bangladesh reported its last polio case due to indigenous wild poliovirus in August 2000. However, there are risks of polio outbreaks following importation because of having over 153 million low socio-economic populations, had history of polio outbreaks following importation in the past (2006) which had resulted 18 polio cases from 12 districts (country has 64 districts). It holds 2nd largest Muslim congregation (Bishwa Ijtima) every year where millions (~5 million) of people joins from more than 70 Muslim countries, including from the polio endemic and/or polio infected countries.

Bangladesh has a very strong surveillance system for polio eradication and consistently maintaining AFP surveillance indicators above certification standard for years. Introduction of environmental surveillance would be a good supplement to the existing AFP surveillance system for early detection of any possible poliovirus importation or emergence of VDPV in the country. In addition, environmental surveillance would also help national programme to monitor presence of type-2 Sabin virus following cessation of type-2 oral polio vaccine from the immunization programme.

12.6.2 National level plan for Environmental surveillance :

The South East Asia Regional Technical Group (TAG) on Immunization in April 2014 has endorsed the plan for expansion of environmental surveillance in the Region. Considering the risk of polio importation and emergence of VDPV case and to supplement existing AFP surveillance system, the National Expanded Programme on Immunization in Bangladesh has planned to introduce environmental surveillance for polioviruses. The national programme also planned to initiate the processes and preparedness for environmental surveillance in 2014 and to implement the environmental surveillance in early 2015. Based on this plan WHO SEAR team joined country team in September 2014 and developed a proposal/plan and started implementing the environmental surveillance from September 2015.

12.6.3 Capacity building of the National polio laboratory:

National polio laboratory has been strengthened by providing necessary equipment and HR development specific for conducting environmental surveillance. At regional level polio lab focal point were trained and regional level provided necessary guidance and support, know how etc. to trained lab focal point to train the laboratory team.

12.6.4 Principles for selecting sewage sampling sites:

Recommended sampling sites are inlets to sewage treatment plants or other major collector sewers. Industrial wastes may contain compounds that may be toxic to cell cultures and/or interfere with poliovirus replication. This has to be taken into account when selecting the sampling sites. In the absence of a sewer network, representative sampling may be difficult to achieve and environmental surveillance should only be started if the major flow routes of wastewater containing human faecal material are sufficiently well known. Targeted, carefully designed stool surveys may be considered as an alternative approach to environmental surveillance in the absence of a sewer network.

Consideration to select sample collection sites includes:

- Sample represents a group of people like 100,000 – 300,000
- Presence of high proportion of high-risk population
- Low vaccination coverage pockets
- Poor sanitation and hygienic status
- Foreign visitors are mainly residing in areas within these zones
- For open drainage system like natural canal/channel, to be free flowing (not stagnated or close canal/channel) and sample to be collected a kilometer prior it gets diluted with other natural channel (like river/lake)
- Site may be reviewed based on laboratory findings as decided the by national programme.

12.6.5 Method of Environmental sample collection:

The plan should clearly indicate who is responsible for collecting the samples at each sampling site. Sampling can be organized by the local authorities or centrally, through the MOH or NPL, whichever is considered the most suitable alternative for the particular situation.

There are two principal modes of collecting environmental samples for virological analysis, referred to as grab and trap sampling. In the grab method an amount of raw sewage is collected at a selected sampling site, either at one point in time, or, preferably, at different predetermined times to form a time-adjusted composite sample.

Grab sample volumes of one litre are recommended. The larger the volume of sewage analyzed the higher the theoretical sensitivity to detect poliovirus circulation in the source population. In practice volumes larger than 1 litre are difficult to handle in the laboratory and may be replaced by several parallel regular samples. Trap samples are collected by hanging a bag of non-specifically absorbing material in the sewage stream. After one or more days the bag is taken out of the sewage and shipped to the laboratory, where the absorbed material is eluted and analyzed for the presence of (polio)viruses.

Grab sampling is preferred to trap sampling as it is more feasible for quantitative

estimation of detection sensitivity of the system, and long-term experience suggests that programmes exploiting concentrated grab samples detect polioviruses and non-polio enteroviruses more often than those using trap sampling. Whatever the sampling principle, collected samples should be immediately refrigerated and kept cool during transport to arrive at the NPL within 48 hours of collection.

12.6.5.1 Collection of grab specimens of sewage:

The National Environmental Surveillance should contain unequivocal detailed

instructions for the following matters.

Sampling sites and persons responsible for sampling

Sewage specimens may be collected at sewage treatment plants, preferably from the inlet collector canal or, if the source population is considered to be too large, from other major collector sewers in the network. Accessibility of the actual sampling site should be agreed upon with the local concern authorities.

Details and responsibilities for provision of the sample vials to be used

Sturdy sample vials of either glass or plastic with a volume of 1–1.5 litre can be used. They should be cleaned but sterilization is not essential. The form of the vial is not important (i.e. bottle, can, etc.) but it should be sealable and compatible with the container to be used for cold transportation of samples. The vial should have an unequivocal identification code and should be accompanied with a form indicating the sampling site and sampling time.

Sampling procedure frequency and time at each sampling site

Sampling frequency should, preferably, *be twice a month (biweekly), but at least once a month as decided by the programme. Sampling to be continued for at least one year, and preferably three years after last WPV isolation*. If environmental surveillance is prompted by known or suspected reintroduction of WPV or appearance of cases caused by circulating VDPV (cVDPV), the initial plan may cover a shorter period (not less than 12 months) and apply more frequent sampling, targeted to more selected populations. This must always be accompanied by intensified AFP surveillance. Time of collection should be selected based on expected *maximum affluent flow* from communities, which is often *between 6-8 am. Time of sampling also becomes important when the temperature is high, as viruses are expected to be inactivated more rapidly.*

A sample of one litre of raw sewage fluid to be collected in the vial, and the outside of the tightly closed vial wiped with a disinfectant before packaging in a cold transport container.

Transport of specimens

Persons responsible for arranging the transport of specimens to be mentioned by name. The parcel must be kept at 4°C before and during the transport to the laboratory.

12.6.5.2 Collection of specimens of sewage by 'trap' method:

During sampling, special precautions should be taken to prevent cross contamination. In the field a sorbent-bag with sorbent should be fixed using fishing-line so that the bag will be in the stream of water. After exposure for 3–7 days the sorbent-bag should be placed in a separate plastic parcel or sterile flask and transported to the laboratory in a cold bag or cold box. Each sorbent-bag should be labelled (locality, point of sampling, date of beginning of the sampling, duration of exposure). Samples should be kept at +4°C for no more than 24 hours and should be kept cool during transport to the laboratory.

12.6.6 Reporting laboratory results:

Reporting of laboratory results from environmental surveillance to programme and WHO should follow the guidelines of reporting for clinical surveillance with respect to the need for regular reporting of activities and findings as well as immediate reporting of wild poliovirus or VDPV isolation.

12.6.7 Interpretation of results and consequences:

The route of poliovirus from an infected individual through the environment to the cell cultures at NPL is very complex, and thus the results obtained in environmental surveillance to be interpreted with caution. A useful criterion of satisfactory overall performance of the surveillance is detection of non-polio enteroviruses in the samples. At least 30% of concentrated sewage from grab samples should reveal NPEV. In populations immunized with OPV, environmental surveillance should also reveal SL strains, especially during and after NIDs and other campaigns.

Abundant OPV-derived strains in the sewage may theoretically mask the presence of small amounts of wild poliovirus if the standard techniques without specific selective conditions for wild poliovirus are being used. However, there is plenty of evidence from practical experience of successful isolation of wild poliovirus during and immediately after NID, and hence there is no need to interrupt environmental surveillance because of an OPV campaign.

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4. *https://polioeradication.org/nopv2/*
5. *https://immunizationdata.who.int/pages/coverage/POL.html?CODE=Global&ANTIGEN=POL3&YEAR=*
6. *http://whqlibdoc.who.int/hq/2003/who_v&b_03.03.pdf*
7. *Polio surveillance database, Bangladesh*
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3. Measles, Rubella & CRS

3.1 Measles

3.1.1 Introduction

Measles is an acute viral infectious disease. References to measles can be found from as early as the 7th century. The disease was described by the Persian physician Rhazes in the 10th century as "more dreaded than smallpox." In 1846, Peter Panum described the incubation period of measles and lifelong immunity after recovery from the disease. Enders and Peebles isolated the virus in human and monkey kidney tissue culture in 1954. The first live attenuated vaccine was licensed for use in the United States in 1963.

3.1.2 Causative agent

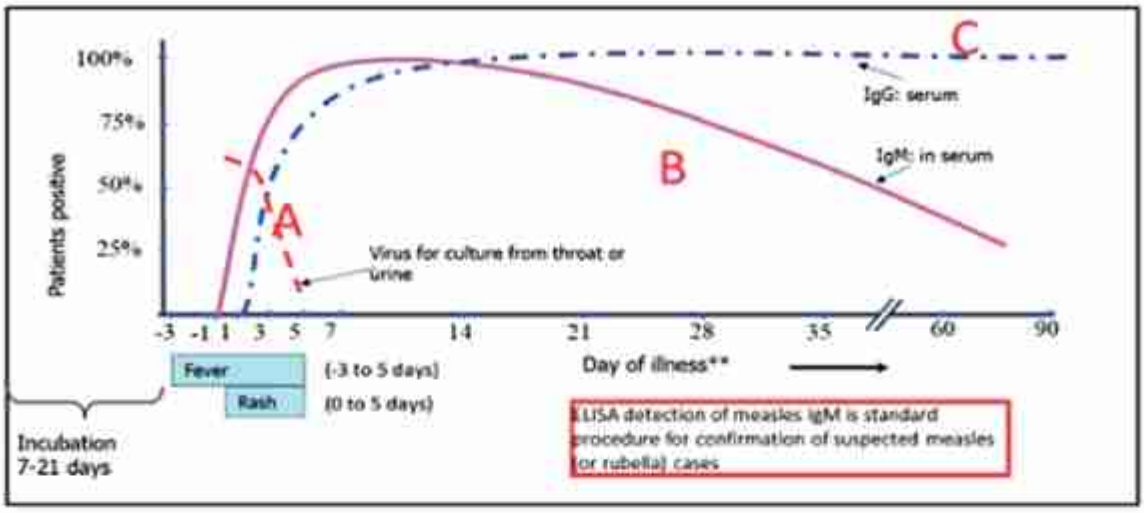
Measles virus is an enveloped, ribonucleic acid (RNA) virus of the genus Morbillivirus, a member of Paramyxoviridae family. Paramyxoviruses are so called because they have an affinity for mucous membranes. It is single-stranded, of negative polarity, and antigenically stable and only one serotype exists. The genome encodes 8 proteins, including the haemagglutinin (H) and the fusion (F) proteins. The lifelong immunity that follows infection is attributed to neutralizing antibodies against the H protein. Sequencing of the measles virus genome has so far identified 24 different genotypes that can be used to track transmission.

It is sensitive to heat and is inactivated rapidly in sunlight, heat and extremes of pH but remains viable over long period when stored at -20°C to -70°C.

3.1.3 Pathogenesis

Measles virus causes systemic infection. The median incubation period is 14 days (range, 7–21 days) from exposure to onset of rash. 2 to 3 days after infection and replication in the respiratory epithelial cells, viruses reach regional lymph nodes and a primary viremia occurs with subsequent spread to the reticuloendothelial system. Following further viral replication in regional and distal reticuloendothelial sites/organs, there is a second wave of viremia, which occurs 5 to 7 days after initial infection. During this secondary viremia, there may be infection of all organs, including the skin, which contributes to the typical rash and the gastrointestinal tract mucosa, which is visible in the oral mucosa as Koplik spots. Measles virus multiplication is more intense now in upper respiratory tract and virus is shed from nasopharynx fluid. Thus, the person is infectious to others from 4 days before rash onset until 4 days after rash onset, the period when the virus spreads into the air as droplets and aerosols). Inhaling such virus results in new hosts getting infected in the community; with the development of immunity, the virus load in the body declines and disappears.

Figure 7: Schematic of wild type measles virus infection



3.1.4 Reservoir

Measles is a human disease. There is no known animal reservoir, no vector and an asymptomatic carrier state has not been documented.

3.1.5 Communicability

Measles is one of the most easily transmitted diseases. It is highly communicable with a secondary attack rate of 75%-90% among susceptible persons. Measles is contagious from the onset of prodromal phase (4 days before rash onset) to 4 days after the rash. The vaccine virus, although it is a live virus, does not appear to be communicable. After infection, the measles virus invades the respiratory epithelium of the nasopharynx and spreads to the regional lymph nodes. After 2 days of replication in these sites, a primary viraemia widens the infection to the reticuloendothelial system. Following further replication, secondary viraemia occurs 5-7 days after infection and last for 4-7 days. The viraemia peaks 11-14 days after infection and then declines rapidly over few days.

3.1.6 Transmission

Measles is a highly infectious (easily transmissible) viral disease spread by direct contact and airborne transmission. If a case of measles is introduced among a group of nonimmune subjects, secondary infection may occur in 12 to 18 persons (Ro= 12–18).

3.1.7 Susceptibility and Resistance

Persons who have not had measles or who have not been successfully immunized are susceptible. Acquired immunity after measles infection is usually life-long. Infants born to mothers who have had measles are immune for periods varying from 3-14 months after birth, depending on the amount of residual maternal antibody at the time of pregnancy and the rate of antibody degradation in the new-born child. The presence of maternal antibody interferes with the infant's immunologic response to measles vaccine.

3.1.8 Prevention

Pre-emptive vaccination is the only rational approach not to have measles disease. Because of the extreme infectiousness of the disease, measures to control outbreaks in highly susceptible communities almost invariably fail.

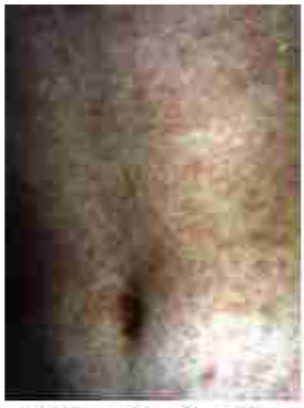
3.1.9 Immunity

Natural measles infection tends to induce higher antibody levels than does measles vaccination. Following infection with measles virus, the initial cell mediated immune response is followed by an antibody mediated response at the time of the rash. Some persons with very low or undetectable antibody titres may be susceptible to measles. Recovery from measles is dependent upon an adequate T-cell response.

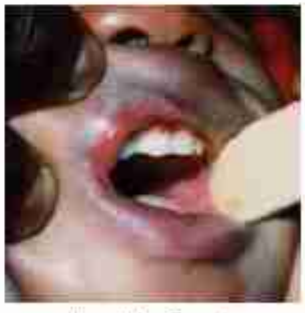
Serologic studies have demonstrated that when given after 9 months of age, the seroconversion rate with measles vaccine is 85%, and after 12 months of age 95%. The peak antibody response occurs 6 to 8 weeks after infection or vaccination. Immunity conferred by vaccination against measles has been shown to persist for at least 20 years and is generally thought to be life-long for most individuals. Depending upon the titre of passively acquired maternal antibodies, young infants are usually protected against measles for several months. This protection decays by 6–9 months of age, leaving infants increasingly susceptible to measles. Therefore, the recommended age for measles vaccination in National immunization schedule is after completion of 9 months followed by 2nd dose after completion of 15 months of age. In emergency settings like FDMN camps while campaign MR vaccine given is at 6 months of age.

3.1.10 Clinical feature of Measles

The incubation period of measles, from exposure to prodrome averages 10-12 days, from exposure to rash onset averages 14 days (range 7–18 days). The prodrome lasts 2-4 days (1-7 days). It is characterized by fever which increases in stepwise fashion, often peaking as high as 103^{0} -105^{0}F followed by cough, coryza and conjunctivitis. Koplik spots appear 1-2 days before the rash to 1-2 days after the rash. It is punctate blue-white spots on the bright red background in the buccal mucosa which are pathognomonic of Measles. The maculopapular rash (measles rash) appear after another 3-4 days, spreads from the face and neck to the trunk and extremities, fading after about 3 days. Patients normally improve by the third day of rash, and are full recovery occurs 7–10 days from the onset of disease. Other symptoms of measles include anorexia, diarrhoea especially in infants and generalized lymphadenopathy.

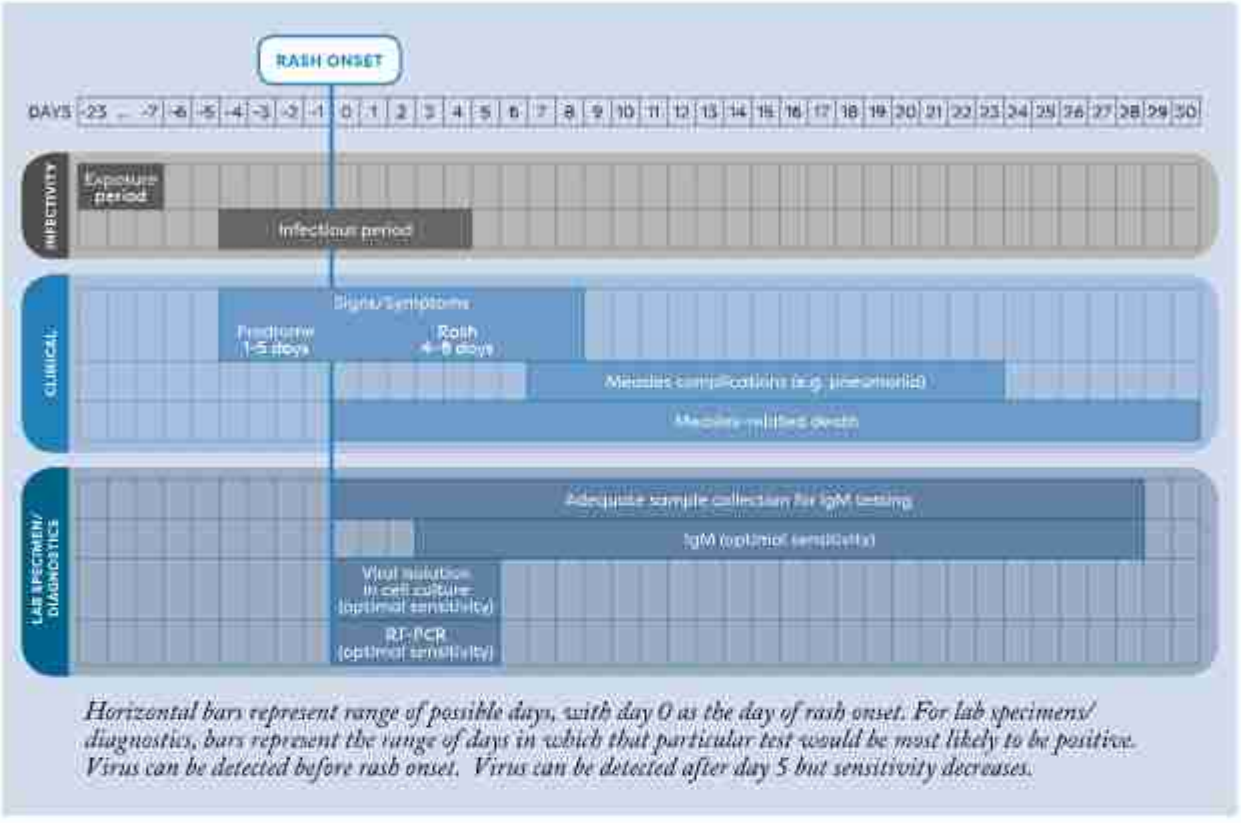


Maculopapular rash



Koplik's Spots

Figure 8: Timeline of Infectivity, clinical disease and laboratory findings for measles virus infection



Horizontal bars represent range of possible days, with day 0 as the day of rash onset. For lab specimens/ diagnostics, bars represent the range of days in which that particular test would be most likely to be positive. Virus can be detected before rash onset. Virus can be detected after day 5 but sensitivity decreases.

3.1.11 Complication

Most persons recover from Measles without sequelae. Some complications associated with Measles may be facilitated by the transient suppression of cellular immunity, which is a characteristic feature of the disease. However, severe forms of the disease, including bleeding from skin and mucosa, may occur. Among children less than 5 years of age, frequent measles complications include otitis media (5–15%) and pneumonia (5–10%). In developing countries, persistent diarrhoea with protein-losing enteropathy may ensue, particularly in young infants.

Measles encephalitis, which is considered an autoimmune disorder, occurs one in about 1000 cases; Subacute Sclerosing Pan encephalitis (SSPE), a slowly progressive infection of the central nervous system, occurs one in about 100,000 Measles cases.

3.1.12 Case Fatality ratio (CFR)

In developed countries, measles deaths are rare, with case-fatality ratios in the range of 0.01-0.1%. In developing countries, the case fatality rate has been estimated in between 5%-15% Persons with malnutrition, especially vitamin A deficiency or with severe immunological disorders such as advanced HIV infection are at increased risk of developing severe or even fatal measles.

3.1.13 Differential Diagnosis

Many illnesses are accompanied by fever, rash and a variety of nonspecific symptoms. In examining for measles, it is important to consider Rubella, Dengue fever, Roseola (Human herpes virus), Erythema Infectiosum (human parvovirus) Enterovirus or Adenovirus infections, Toxic shock syndrome, Rickettsial diseases and drug hypersensitivity reaction

Differential Diagnosis

- Rubella
- Dengue fever
- Roseola
- Erythema Infectiosum
- Enterovirus /Adenovirus infection
- Drug hpersensitivity

Table 3: Comparison of clinical and epidemiological characteristics of measles and its differential diagnosis

Disease	Rubella	Measles	Dengue	Erythema infectiosum	Roseola infantum
Causative agent	Rubella Virus	Measles Virus	Dengue Virus	Parvo virusB1	Human Herpes6
Incubation Period	14-23	7-18	2-12	4-20	10
Fever	Yes	Yes	Yes	Yes	Yes
Rash	Yes	Yes	Yes	Yes	Yes
Conjunctivitis	Yes	Yes	Yes	Yes	No
Coryza	Yes	Yes	Yes	Yes	No
Joint symptoms	Yes	No	Yes	Yes	No
Retro auricular lymphadenopathy	Yes	No	No	No	Yes
Serological test	IgM	IgM	IgM	IgM	IgM
Still births	Yes	Yes	Yes	Yes	No
Birth defects	Yes	No	No	No	No

3.1.14 Measles Vaccine

Measles vaccine consists of live, attenuated strains of measles virus and is available, either as monovalent measles vaccine or as measles-containing vaccine (MCV) in combination with rubella, mumps or varicella vaccines. When using the combined measles–rubella (MR) vaccine, measles–mumps–rubella (MMR) vaccine or measles–mumps–rubella–varicella (MMRV) vaccine, the protective immune responses to each individual vaccine antigen as well as vaccine-associated adverse events remain largely unchanged. However, the rate of febrile seizures occurring 7–10 days after the first dose in children vaccinated with MMRV is about 2 times higher (9/10,000) than in children who receive MMR and varicella vaccines separately at the same visit.

Measles vaccine protects equally well against all wild measles virus genotypes. A live vaccine virus does not spread from vaccinated to the unvaccinated.

Immune responses to Measles Containing Vaccine (MCV): Measles vaccine induces both humoral and cellular immune responses comparable to those following natural infection, although antibody titres are usually lower. Following vaccination, transient measles-specific immunoglobulin (Ig) M antibodies appear in the blood and IgA antibodies appear in mucosal secretions; IgG antibodies, hence protective immunity, persist for decades. Vaccination also induces measles virus specific CD4+ and CD8+ T lymphocytes.

Vaccinating infants before or at the age of 6 months often fails to induce seroconversion due to the immaturity of the immune system as well as the presence of neutralizing maternal antibodies. The development of a high avidity antibody response is critical to the development of protective immunity to measles virus. Antibody avidity to measles virus is generally lower in children vaccinated at age 6 to 9 months compared with the avidity obtained in children vaccinated at age 12 months or above.

Studies on revaccination in children who failed to respond to their first dose of measles vaccine given at 12 months show that almost all develop immunity after their second dose. Although vaccine-induced antibody concentrations decline over time and may become undetectable, immunological memory persists and, following exposure to measles virus, most people who have been vaccinated produce a protective immune response.

Following vaccination, the long-term persistence of neutralizing measles antibodies (26–33 years) and long-lasting protection against measles have been demonstrated by several investigators. No studies yet have identified declining immunity as an important risk factor.

3.2 Rubella

3.2.1 Introduction:

The name rubella is derived from latin, meaning "little red". Initially it was considered to be varient of measles or scarlet fever and was called 'third disease". In 1814, it was first described as a separate disease in the German medical literature, hence the common name "German measles". Following a widespread epidemic of rubella infection in 1940, Norman Gregg, an Australian opthalmologist, reported in 1941 the occurance of congenital rubella syndrome.

Rubella is an acute, usually mild illness that presents exanthematous fever and rash ,affecting susceptible children and young adults worldwide. Its public health importance is due mainly to the teratogenic potential of the virus. Infection in the early months of pregnancy usually affects foetal development. Rubella infection of the foetus can result in miscarriage, foetal death or birth of an infant with serious congenital defects. Congenital Rubella Syndrome (CRS) is an important cause of blindness, deafness, congenital heart disease and mental retardation.

3.2.2 Causative agent

Rubella virus is the only member of the Rubivirus genus of the Togavirus family. It is an enveloped RNA virus, with a single antigenic type that does not cross -react with other members of the togavirus group. It is relatively temperature labile but is more heat stable than measles virus. Rubella virus is inactivated after 30 minutes at 56°C, 4 minutes at 70°C and 2

minutes at 100°C. It is also susceptible to a wide range of disinfectants and is inactivated by 1% sodium hypochlorite,70% ethanol and formaldehyde.

3.2.3 Pathogenesis

Following respiratory transmission of rubella virus, replication of the virus occurs in the nasopharynx and regional lymph nodes. The incubation period is 18 days (range 12 to 23 days). Viremia occurs 5–7 days after infection and results in viral spread to different organs. Rubella virus can be found in nasopharyngeal samples from 1 week before the onset of the rash to 2 weeks after, with maximal shedding occurring 1–5 days after rash onset. In pregnant women, transplacental infection of the fetus occurs during viremia. The virus infects the developing fetus. Fetal damage occurs through destruction of cells as well as mitotic arrest. Infants born with congenital rubella may shed the virus for a year or more in pharyngeal secretions and urine.

3.2.4 Reservoir

There is no known animal reservoir. Infants with CRS may shed rubella virus for an extended period. Post-natal infection does not lead to prolonged shedding.

3.2.5 Communicability

Rubella spreads through contact with nasal or throat secretions of an infected person. This may result from airborne droplet spread, direct contact with an infected person or indirect contact with freshly infected articles. Infants with CRS shed large quantities of rubella in their pharyngeal secretions and in urine, can serve as a source of transmission.

Rubella is moderately contagious, mostly when the rash is erupting, but is communicable from 1 week before, to 5-7 days or more after the onset of the rash. Infants with CRS may shed virus up to year after birth. There is no evidence that the vaccine virus can spread to contacts.

3.2.6 Transmission

Transmission is primarily by large droplets spread or direct contact with nasal or throat secretions from an infected person. Less commonly it spreads by airborne aerosolized droplet nuclei or by indirect contact with freshly contaminated articles.

After the rubella virus infects the nasopharynx, it multiplies in the lining of the respiratory tract and in local lymph nodes before passing in to the blood stream. Viremia begins 5-7 days after infection, spreading throughout the rest of the body, including skin. Virus can be isolated from the nasopharynx from up to 1 week before, to up to 2 weeks after the onset of rash.

3.2.7 Susceptibility and Resistance

Humoral and cell mediated immunity develop following a rubella infection. IgG and IgM antibodies are observed about 14-18 days after rubella infection, at about the time when the rash appears. Rubella IgM antibody wane quickly and are usually undetectable after 2 months, whereas rubella IgG antibody persists.

Rubella specific IgM is diagnostic of acute infection. Rubella specific IgG is a long-term marker of previous rubella infection. IgG begins to rise after the onset of the rash, peaks about four weeks later and generally lasts for rest of life. Natural rubella infection generally confers lifelong immunity.

3.2.8 Prevention

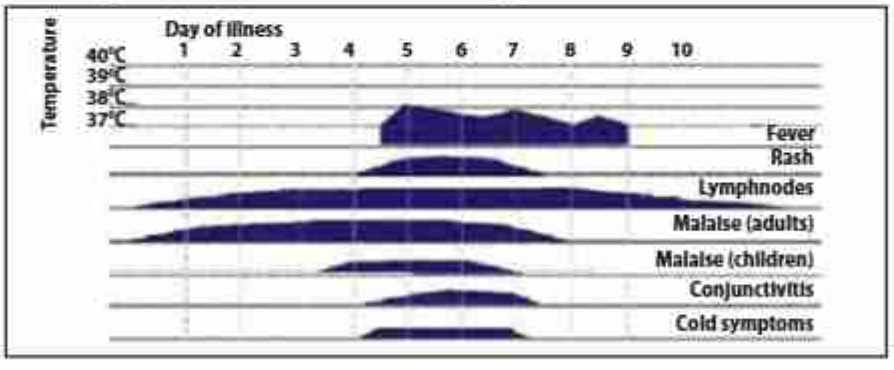
Vaccination is the rational approach not to have Rubella. One does of rubella containing vaccine on or after the first birthday is effective tool for controlling rubella

3.2.9 Clinical Aspects of Rubella

Approximately 50% of rubella infections are subclinical and may not be detected except through laboratory confirmation. The main symptoms include inflammation of the lymphnodes and a maculopapular rash, which may be preceded by mild catarrhal symptoms. Enlargement of the lymphnodes (lymphadenopathy) occur from 5-7 days before and up to 2 days after the onset of rash.

The incubation period for rubella ranges from 12-23 days, average period is 14 days. A short prodromal phase (1-5 days) occurs before the rash appear in adolescents and adults but not in children. In children rash is usually the first manifestation. The prodrome involves low grade fever, headache, malaise, anorexia, mild conjunctivitis, coryza, sore throat, cough and lymphadenopathy involving the suboccipital, post auricular and cervical lymphnodes. Approximately 14-18 days after infection, a maculopapular rash develops. The rash, which may be difficult to see, starts on the face and neck and spreads rapidly down over the trunk and extremities. The rash fades after 1-3 days and is occasionally pruritic. Joint pain and temporary arthritis, which are uncommon in children, occur frequently in adults, especially in women.

Figure 9: Clinical features of typical rubella infection



3.2.10 Clinical feature of Rubella

Rubella is a mild self-limited illness that usually occurs during childhood. During the second week after exposure, there may be a prodromal illness consisting of fever usually <39.0 °C, malaise and mild conjunctivitis, which is more common in adults. Post auricular, occipital and posterior cervical lymphadenopathy is characteristic, and typically precedes the rash by 5–10 days. The maculopapular, erythematous and often pruritic rash occurs in 50–80% of rubella-infected persons. The rash, usually lasting 1–3 days, starts on the face and neck before

progressing down the body. Serological studies have shown that 20–50% of all rubella infections occur without a rash, or are subclinical. Joint symptoms (arthritis, arthralgia), usually of short duration,

3.2.11 Complication

Complications of rubella are not common, but they generally occur more often in adults than in children.

Arthralgia or arthritis affects often fingers, wrists and knees. Joint symptoms tend to occur about the same time or shortly after appearance of rash and may last up to one month. Chronic arthritis is rare.

Encephalitis occurs in one in 6000 cases, more frequently in adults especially in females than children, but occasionally incidences have been reported as high as 1/500 and 1/1600. Mortality estimates vary from 0 to 50%.

Haemorrhagic manifestations occur in approximately one per 3,000 cases, occurring more often in children than in adults. These manifestations may be secondary to low platelets and vascular damage, with thrombocytopenic purpura being the most common manifestation. Gastrointestinal, cerebral or internal haemorrhage may occur. Effect may last from days to months, and most patients recover. Additional complications include orchitis, neuritis, and a rare late syndrome of progressive panencephalitis.

3.2.12 Laboratory Diagnosis

Many rash illnesses can mimic rubella infection, and as many as 50% of rubella infections may be subclinical. The only reliable evidence of acute rubella infection is a positive viral culture for rubella or detection of rubella virus by polymerase chain reaction (PCR), the presence of rubella-specific IgM antibody or demonstration of a significant rise in IgG antibody from paired acute- and convalescent-phase sera.

Rubella virus can be isolated from nasal, blood, throat, urine and cerebrospinal fluid specimens from rubella and CRS patients. Virus may be isolated from the pharynx 1 week before and until 2 weeks after rash onset. Although isolation of the virus is diagnostic of rubella infection, viral cultures are labour intensive and therefore not done in many laboratories; they are generally not used for routine diagnosis of rubella. Viral isolation is an extremely valuable epidemiologic tool and should be attempted for all suspected cases of rubella or CRS.

Serology is the most common method of confirming the diagnosis of rubella. Acute rubella infection can be serologically confirmed by a significant rise in rubella antibody titre in acute- and convalescent-phase serum specimens or by the presence of serum rubella IgM. Serum should be collected as early as possible (within 7–10 days) after onset of illness, and again 14–21 days (minimum of 7 days) later. False-positive serum rubella IgM tests have occurred in persons with parvovirus infections, with a positive heterophite test for infectious mononucleosis, or with a positive rheumatoid factor.

The serologic tests available for laboratory confirmation of rubella infections vary among laboratories.

Enzyme-linked immunosorbent assay (ELISA) is sensitive, widely available and relatively easy to perform. It can also be modified to measure IgM antibodies. Most of the diagnostic testing done for rubella antibodies uses some variation of ELISA.

Serological testing is the preferred method for routine laboratory diagnosis of rubella. The presence of rubella IgM or demonstration of a significant rise in rubella IgG from paired acute and convalescent serum samples provides evidence of ongoing or recent rubella infection. On rare occasions, false-positive IgM results may occur when IgM antibody detection kits are used, e.g. enzyme-linked immunosorbent assay (ELISA). Where rubella is rare, false-positive serological results become relatively more common, thereby increasing the need for confirmatory tests. The presence of IgM antibody must always be interpreted with caution if there is no clear clinical context (e.g. when testing is routinely performed during pregnancy). Congenital rubella infection is most commonly diagnosed by detection of rubella IgM in serum or oral fluid sampled during the early months of life.

Currently, ELISA is the most frequently used method for rubella antibody screening and diagnosis because it is sensitive and adaptable and can be readily automated. However, the majority of early studies on rubella vaccines and seroprevalence studies used a haem agglutination inhibition assay. Latex agglutination, single radial haemolysis and plaque neutralization may also be used, mainly for confirmatory purposes. RT–PCR assay is a highly sensitive and specific diagnostic tool. Viral isolation is labour-intensive and costly, and is not routinely used for diagnosis.

3.2.13 Treatment

There is no effective antiviral treatment for rubella, and symptoms are often so mild that treatment usually is not necessary. However, isolation from others especially pregnant women during the infectious period is necessary. Treatment of symptoms includes plenty of fluids and pain relief if required. Paracetamol may be used to reduce fever and pain. Aspirin should not be given to children under 12 years of age unless specifically recommended by a doctor.

3.2.14 Rubella Vaccine

The Rubella RA 27/3 vaccine is a live attenuated virus, was first isolated in 1965. The virus was attenuated by 25-30 passages in tissue culture, using human diploid fibroblasts. It does not contain duck, chicken or egg protein. There are a few other vaccines based on different strains available in some other regions. Rubella vaccines are available either as monovalent formulations or in combinations with other vaccine viruses, as RCVs. Commonly used RCVs are combinations with vaccines against measles (MR), measles and mumps (MMR) or measles, mumps and varicella (MMRV). Each dose of an RCV contains a defined number of infectious units (≥1000 PFU or CCID50). When stored at +4 °C, most RCVs have a shelf-life of 2–3 years.

Schedules

The high response rate to a single dose of rubella vaccine (≥95%) and the long-term persistence of protection in vaccines do not support a routine requirement for a second dose of rubella vaccine. However, based on the indications for a second dose of measles-containing and mumps-containing vaccines, a second dose of MR or of MMR is now offered in most countries.

An RCV is normally administered as a subcutaneous injection (but may also be given intramuscularly), usually at age 12–15 months, but it can also be administered to children aged 9–11 months and to older children, adolescents and adults. In most countries, rubella vaccine is given as MR or MMR, and the age of administration follows the schedule for measles – that is, the first dose is usually given 9 months or 12–15 months and a second dose at 15–18 months or 4–6 years.

During outbreaks of measles, MR or MMR may be administered to infants as young as 6 months. Because of the possibility of lower seroconversion, the dose administered at 6 months should not be counted as a valid dose, and the child should be vaccinated with subsequent dose(s) of RCVs according to the usual national immunization schedule.

Immunogenicity and vaccine efficacy

Rubella vaccine induces seroconversion rates of approximately 95% or higher after a single dose.

The RA27/3 strain achieves antibody titres that closely resemble those induced by natural infection. In clinical trials, 95–100% of susceptible persons aged 12 months and older developed rubella antibodies after a single dose of the vaccine. It should be noted, however, that the immune response may be relatively slow, and therefore, it is advisable to wait until 6–8 weeks after immunization to assess seroconversion. Up to 5% of all vaccines fail to seroconvert; in part, this may be due to concurrent infection or – in young infants – to pre-existing maternal rubella antibodies.

The immune responses to rubella antigens are not affected by the other components of the vaccine in the combinations MR, MMR or MMRV. Also, seroconversion rates are similar among the different formulations of RA 27/3 vaccine when it is given concurrently with other live or inactivated vaccines.

3.3 Measles and Rubella surveillance

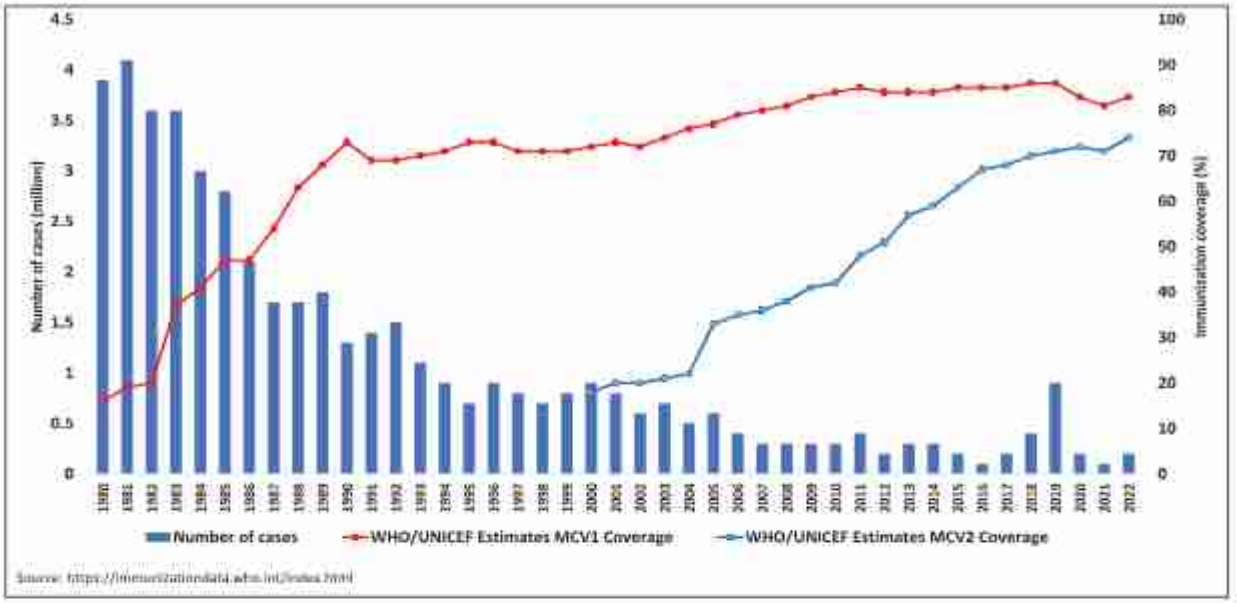
3.3.1 Background

In May 2012, at the World Health Assembly (WHA), the Global Vaccine Action Plan (GVAP) of the decade of vaccines (DoV) was endorsed. One of the goals of GVAP was to meet measles and rubella elimination in at least 5 Regions by 2020.

In 2013, at the 66th session of the Regional Committee of the World Health Organization (WHO) South-East Asia Region (SEAR), the 11 SEAR member states established a regional goal to eliminate measles and control rubella and congenital rubella syndrome (CRS)* by 2020. Country efforts in the South-East Asian Region have led to a 75% decline in measles deaths between 2000 and 2017. Based on the recommendations of the midterm review and regional verification Committee (SEAR-VC) for measles elimination and control of rubella & CRS, the 72nd session of the Regional Committee of the WHO South-East Asia Region (SEAR) adopted the target of elimination of measles and rubella by 2023.

The impact of the measles vaccine on global public health is tremendous. Before 1963, most of the world's population caught measles by their 15th birthday, resulting in an estimated 100 million cases and over 2 million deaths annually. By 2000, four decades of steadily increasing use of the vaccine saw a dramatic reduction of cases to just over half a million annually. In 2002, the Americas declared that measles was eliminated from the region.

Figure 10: Measles global annual reported cases and MCV1 coverage, 1980-2022



Some Key facts

- Even though a safe and cost-effective vaccine is available, in 2018, there were more than 140 000 measles deaths globally, mostly among children under the age of five.
- Measles vaccination resulted in a 73% drop in measles deaths between 2000 and 2018 worldwide
- In 2018, about 86% of the world's children received one dose of measles vaccine by their first birthday through routine health services – up from 72% in 2000.
- During 2000- 2018, measles vaccination prevented an estimated 23.2 million deaths making measles vaccine one of the best buys in public health.

3.3.2 Measles and Rubella Surveillance in Bangladesh

In setting a measles elimination goal, a sensitive case-based surveillance system is essential to monitor progress toward elimination and to sustain measles, rubella and CRS elimination. The objectives of case-based surveillance are to detect, investigate and classify all suspected cases; and to respond confirmed outbreaks. Bangladesh started measles outbreak surveillance in 2003 and case-based surveillance from 2008. Currently Bangladesh is conducting 'fever and rash' surveillance to detect measles and rubella, under which all the samples collected are tested for both measles and rubella (parallel testing).

The objectives of surveillance are to:

- Characterize epidemiology and measure burden of measles and rubella
- Detect and investigate outbreak and take immediate actions for preventing additional cases or deaths during outbreaks
- Help public health officials at the upazila, district, municipality, city corporation, division and national level to develop more effective strategies to prevent diseases
- Measure the impact of vaccination programme
- Identify high risk population and areas
- Identify problems in service delivery (e.g. Cold chain problem, adverse event)

- Measure the impact of specific health interventions and determine if a particular disease prevention strategy is effective (e.g. supplementary vaccination campaigns).

The standard mode of surveillance for elimination strategies is to detect, report and investigate all suspected cases; for case confirmation, laboratory testing at an accredited laboratory is crucial. As Bangladesh is moving toward elimination goal hence, the laboratory-supported case-based surveillance is vital for better understanding of transmission patterns and guide rapid response to interrupt the chains of virus transmission.

3.3.3 Measles Elimination in Bangladesh

Bangladesh endorsed the measles mortality reduction goal set in UN General Assembly Special Session on children in May 2002 and in World Health Assembly 2003. In accordance with the Joint WHO/UNICEF measles mortality reduction strategic plan, the Government of Bangladesh developed the National Measles Control Plan of Action 2004-2010. Based on the plan, measles catch-up campaign was conducted targeting 35 million children from 9 months to 10 years in 2005-06, followed by follow up campaign in 2010 targeting 9 months to under 5 years children and MR campaign in 2014 targeting 9 months to under 15 years children. The last MR follow up campaign was conducted from December 2020 – February 2021 where more than 36 million children were vaccinated.

In line with regional goal Bangladesh is determined to eliminate measles, rubella and CRS by 2023. Bangladesh has started measles surveillance integrated with VPD (Vaccine Preventable Diseases) surveillance from 2003 and initiated measles case-based surveillance from 2008. CRS surveillance was initiated in 2012 and CRS surveillance integrated with AFP and VPDs surveillance from 2014. Bangladesh has made significant progress in achieving sensitive and quality measles surveillance.

Measles vaccine was introduced in Bangladesh in 1979. Since 1979-2011 single dose of measles vaccine was given after completion of 09 months of age. Rubella vaccine was introduced as first dose of combination of Measles-Rubella (MR) vaccine in 2012. In the same year measles 2nd dose was introduced after completion of 15 months of age. Measles second dose was replaced by MR second dose in 2015.

The epidemiology of measles, rubella and CRS in Bangladesh suggests that the country is making progress towards their eventual elimination. Following the 2014 catch-up MR SIA, the number of measles and rubella outbreaks dropped sharply during 2014 and 2015 (figure 11). Similarly, the actual number of rubella cases dropped dramatically and has remained low (figure 14) with annual incidence of 0.75 – 1.2 confirmed cases per million population since 2014. However, the number of measles outbreaks has picked up in 2017, 2018 & 2019 which dropped again after the MR campaign 2020.

Figure 11: Confirmed measles and rubella outbreaks, by district and year, Bangladesh 2018-2022

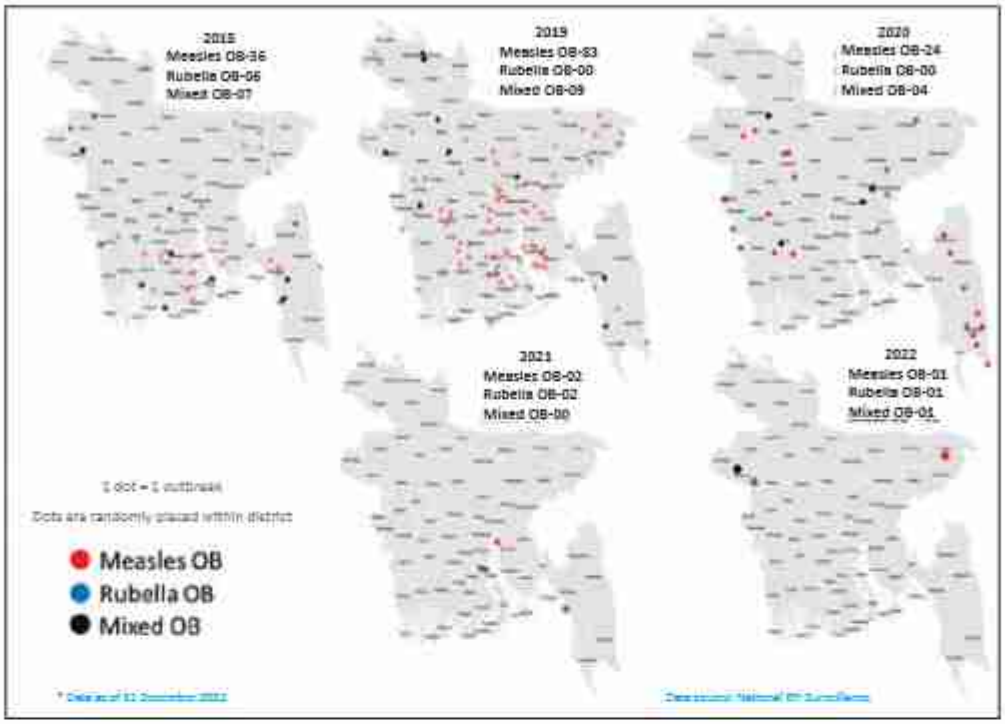


Figure 12: Confirmed measles cases, Bangladesh 2018-2022

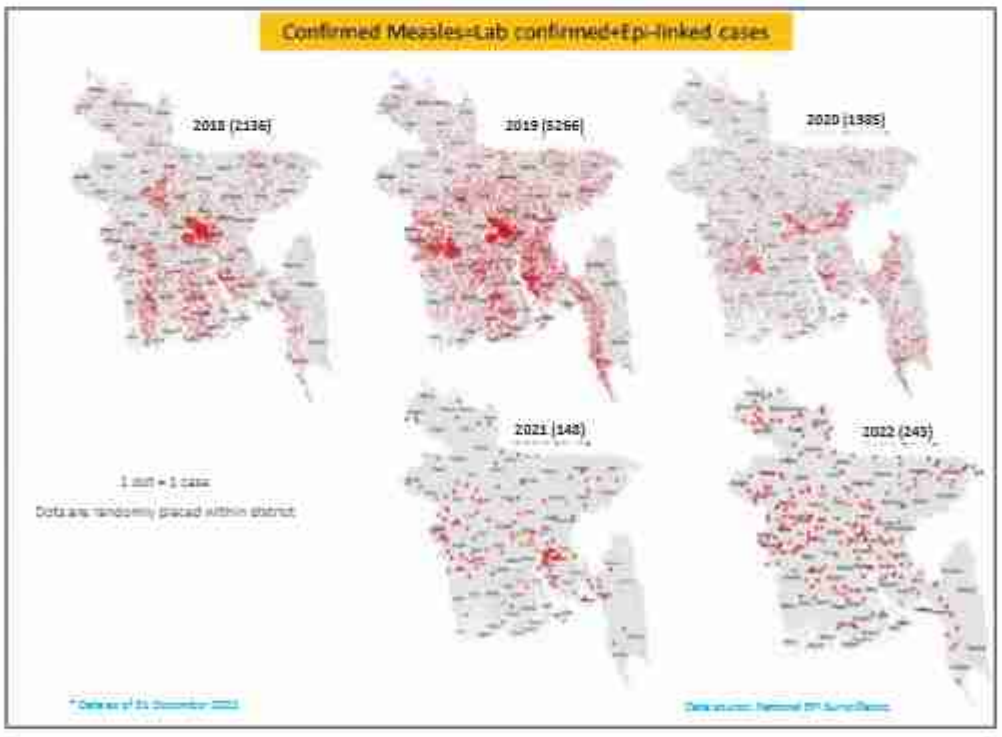


Figure 13: Annualized incidence of confirmed measles by districts and year, 2018-2022

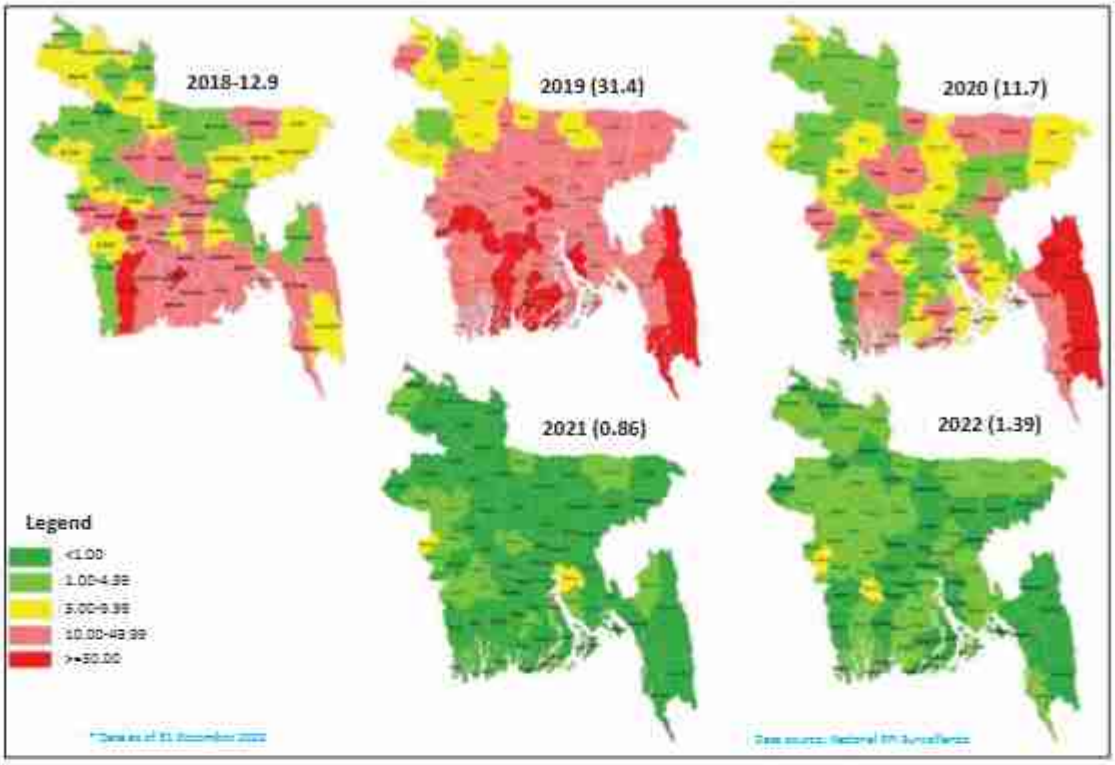


Figure 14: Confirmed rubella cases, Bangladesh 2018-2022

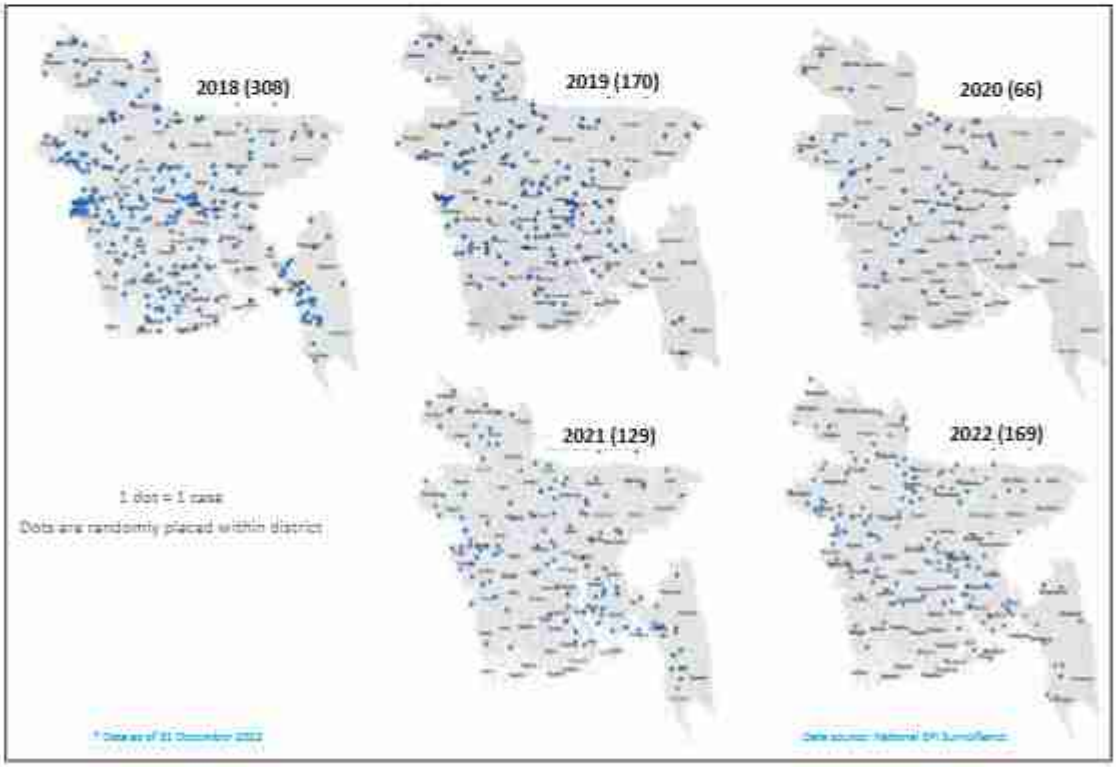
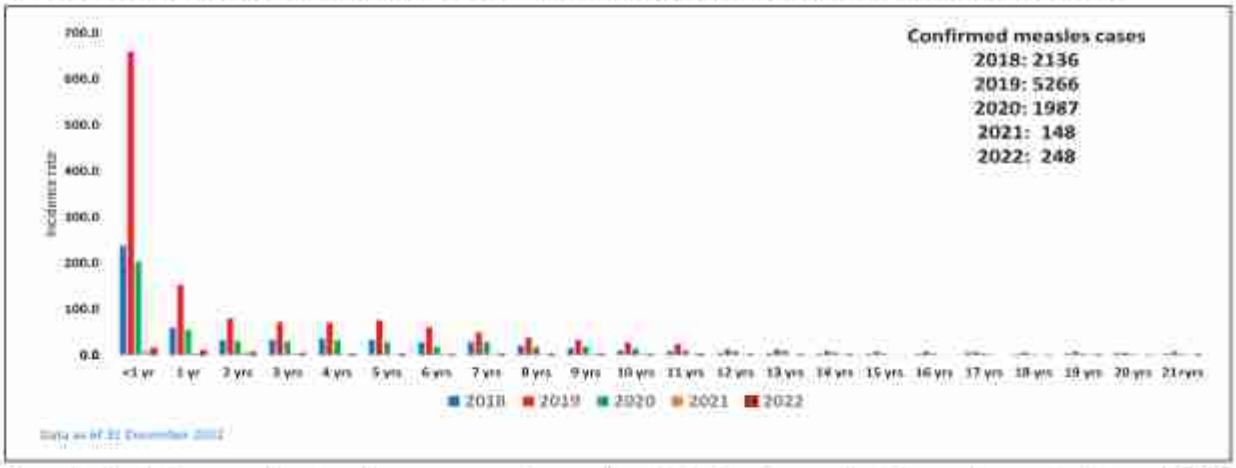


Figure 15: Age specific incidence of confirmed measles cases, 2018-2022, Bangladesh



Bangladesh has made steady progress towards achieving its goal of measles, rubella and CRS elimination with respect to increasing levels of population immunity over wide age-ranges, surveillance quality and routine vaccination coverage with two doses of MR vaccine. However, reaching the last 5-10 percent of children that remain unvaccinated or under-vaccinated remains a common challenge for this and all immunization programmes. Such children are often the hardest to reach. Rigorous and uniform application of the proven measles and rubella elimination strategies, in addition to developing and

implementing innovative tactics for specific populations and situations, are necessary to achieve the equity and timeliness of vaccination service delivery and utilization as well as elimination-standard surveillance quality that are needed to achieve and sustain measles, rubella and CRS elimination.

The Government of Bangladesh has endorsed a National strategic Plan of Action by adopting the global and regional strategies to address the issue of measles and rubella burden.

3.3.3.1 Goal of Measles, rubella & CRS

Achieve and maintain elimination of measles and rubella with interruption of the transmission of indigenous measles and rubella viruses by 2023.

Objectives

1. Achieve and maintain at least 95% coverage with 2 doses of MR vaccine in every upazila, municipality and city corporation zone through routine and/or supplementary immunization.
2. Establish elimination standard measles, rubella and CRS surveillance and programme performance monitoring.
3. Maintain an accredited measles and rubella laboratory to conduct serologic and virologic/molecular testing for measles, rubella and CRS.
4. Prevent, prepare and respond to measles and rubella outbreaks.
5. Advocacy, social mobilization and program communication to obtain political commitment for measles, rubella and CRS elimination, establish inter-sectoral and societal linkages and create demand for immunization services.

3.3.3.2 Strategies of Measles Elimination Programme

Four strategical components

- Strong routine immunization: The first dose of measles containing vaccine (MCV1) is given to the children at the age of 9 months (i.e. after completion of 9 months to before the first birthday)
- Second opportunity for measles immunization: A second dose of measles vaccine (MCV) is given to all children at the age of 15 months (i.e. after completion of 15 months) through routine immunization aiming to vaccinate all children of target age group.
- Intensified surveillance: prompt identification and investigation of measles cases with sample collection for laboratory confirmation
- Improved clinical management of measles cases: providing Vitamin A supplementation and adequate treatment of complications.

3.3.4 Case definition and case Classification

Suspected case of measles: A patient with *fever and maculopapular (non-vesicular) rash* or a patient whom a clinician suspects measles or rubella irrespective of age.

Suspected Measles Outbreak: Occurrence of 3 or more cases in a rural ward or urban mahalla (approximately 10,000 population) in a period of 30 days. A single laboratory confirmed case of measles or rubella should be treated as an outbreak and public health response should be initiated accordingly.

Laboratory criteria for diagnosis: Presence of measles/rubella specific IgM antibodies.

Laboratory-confirmed case: A suspected case of measles or rubella that has been confirmed positive by testing in a proficient laboratory, and vaccine-associated illness has been ruled out.

Epidemiologically linked case: A suspected case of measles, or rubella, that has not been confirmed by a laboratory but was geographically and temporally related, with dates of rash onset occurring 7–21 days apart for measles (or 12–23 days for rubella) to a laboratory-confirmed case or, in the event of a chain of transmission, to another epidemiologically-confirmed measles or rubella case.

Clinically compatible measles case: A suspect case with fever and maculopapular (non-vesicular) rash, for which no adequate clinical specimen was taken and which has not been linked epidemiologically to a laboratory-confirmed case of measles, rubella or another laboratory-confirmed communicable disease.

As countries get closer to elimination, most of the suspected measles cases should be confirmed by laboratory or epidemiological linkage. Clinically compatible cases are highly unlikely to be measles when the country is at or near elimination.

Clinically compatible rubella case: As the rubella surveillance of Bangladesh is utilizing the measles surveillance platform, there is no clinically compatible rubella cases rather clinically compatible measles case.

Non-measles discarded case: A suspected case that has been investigated and discarded as non-measles using laboratory testing in a proficient laboratory or epidemiological linkage to a

laboratory-confirmed outbreak of another communicable disease confirmation of another aetiology failure to meet the clinically compatible measles case definition.

If the case is also negative for rubella, this is a non-measles non-rubella discarded case.

Endemic cases: Endemic measles transmission is the existence of any continuous indigenous chain or re-established chain of transmission of measles/rubella virus persisting for >1 year in any defined geographic area. An endemic measles case is a laboratory or epidemiologically confirmed measles case resulting from endemic transmission of the measles virus. For rubella, any case that cannot be proved to be imported is considered indigenous.

Imported cases: An imported measles case is a confirmed case which, as supported by epidemiologic and/or virologic evidence, was exposed outside the country or region during the 7–21 days prior to rash onset. For rubella, the time frame is 12–23 days. A travel history to an area where measles occurs and during a plausible time frame must be demonstrated; results of molecular sequencing of the virus isolated from the cases should be compatible with the areas/countries visited. The possibility of local exposure to measles must be excluded after a careful community investigation.

Import-related cases: An import-related case is a confirmed case which, as supported by epidemiologic and/or virologic evidence, has locally acquired infection as part of a transmission chain related to an imported case. A chain of transmission is two or more confirmed cases that are epidemiologically linked. The investigation should thus demonstrate that the import-related case had direct contact 7–21 days with an imported case or another import-related case (12–23 days before rash onset for rubella). Molecular sequencing data of the isolated virus, if available, could support the link.

Cases with unknown source of infection: A confirmed case for which the source of infection was not identified. It is possible that an epidemiological link to an imported case or an import-related case cannot be found even after a thorough investigation, and sporadic cases with unknown source of infection are not necessarily indicative of endemic transmission. However, the identification of sporadic cases might indicate gaps in surveillance. The pattern of occurrence of these cases (e.g. number of transmission chains and number of cases involved, geographical and temporal distribution) is as important as their number.

Measles vaccine-associated illness:

A suspected case that meets all five of the following criteria:

1. The patient had a rash illness, but did not have cough or other respiratory symptoms related to the rash
2. The rash began 7–14 days after vaccination with a measles-containing vaccine
3. The blood specimen, which was positive for measles IgM, was collected 8–56 days after vaccination
4. A thorough field investigation did not identify any secondary cases
5. Field and laboratory investigations failed to identify other causes, or genotype A was isolated from the suspected case (genotype A is only vaccine-related and does not occur as wild-type infection).

Acute measles-related death: Any death occurring within 30 days of rash onset of a measles case (laboratory-confirmed, epidemiologically linked, clinically compatible) that is related to a complication of measles (such as pneumonia) not due to other related cause. e.g. a trauma or chronic disease.

3.3.5 Key definitions related to measles and rubella surveillance

Measles, or rubella, eradication: worldwide interruption of measles, or rubella, virus transmission in the presence of a surveillance system that has been verified to be performing well.

Measles elimination: the absence of endemic measles transmission in a defined geographical area (e.g. region or country) for ≥12 months in the presence of a well-performing surveillance system. However, verification of measles elimination takes place after 36 months of interrupted endemic measles virus transmission.

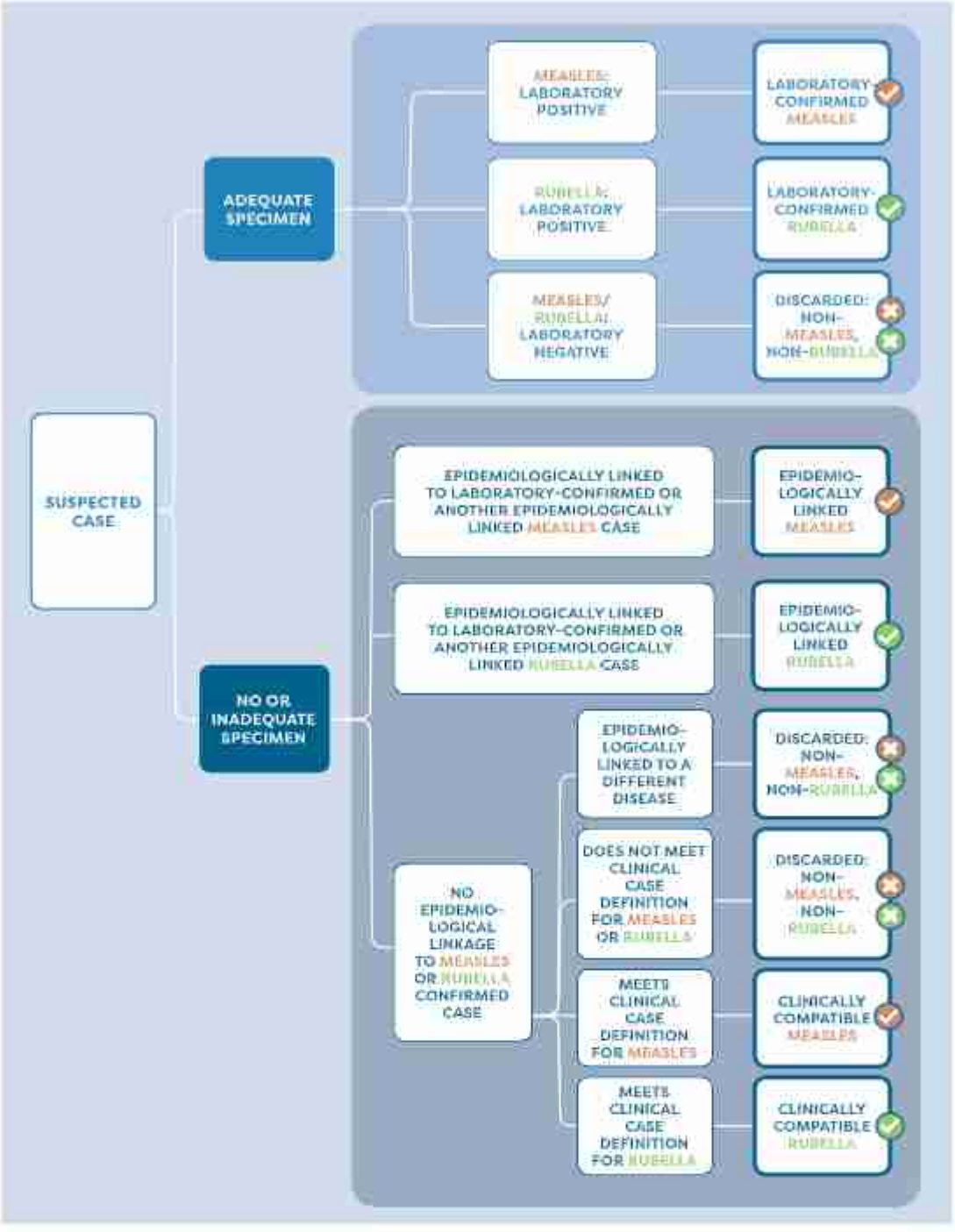
Rubella and CRS elimination: the absence of endemic rubella virus transmission in a defined geographical area (e.g. region or country) for >12 months and the absence of CRS cases associated with endemic transmission in the presence of a well-performing surveillance system. However, verification takes place after 36 months of interrupted endemic virus transmission.

Rubella and CRS control: a 95% reduction of rubella and CRS as compared with the 2008 baseline nationally and for the Region.

Endemic measles, or rubella, virus transmission: the existence of continuous transmission of indigenous or imported measles virus, or rubella virus, that persists for ≥12 months in any defined geographical area.

Re-establishment of endemic transmission: occurs when epidemiological and laboratory evidence indicates the presence of a chain of transmission of a virus strain that continues uninterrupted for ≥12 months in a defined geographical area where measles or rubella had previously been eliminated.

Figure 16: Classification of Suspected measles and rubella cases



Laboratory or epidemiologically confirmed cases should be further classified according to the source of the infection as imported cases, import-related cases or cases with an unknown source.

3.3.6 Measles case Investigation

Case Identification, Notification, Investigation & reporting

In elimination mode, measles surveillance must be case based. The surveillance system should be able to do the following in a timely manner:

- detect, notify and investigate suspected measles cases and outbreaks; correctly classify cases as confirmed or discarded; determine if they were due to failure of programme implementation (for example, should have been vaccinated but were not), due to vaccine failure, or occur in someone for whom vaccination is not recommended; and inform actions that reduce morbidity and mortality and prevent further virus transmission.
- Active surveillance in health facilities: All cases of measles who meet the surveillance case definition of measles when present to the outpatient clinic, emergency room and inpatient ward in health care facilities should be identified and investigated by attending physician. The clinicians (RMOs, MOs, Paediatricians and other Physicians) of the health care facility collect information from cases when they attend the patients for first time. They record information on AFP & EPI disease report form *(Annexure 01)* and hand over to HSO at the end of their duty.
- Passive Surveillance: Weekly review of health facilities register book is essential so that no case is missed. In Bangladesh the surveillance system is established in selected health facilities (both private and public) throughout the country.
- Medical officer in the hospital detects, investigates and reports any suspected measles cases to HSO immediately using "Suspected measles case investigation form" *(Annexure 09)*. S/he also must assist in collection of specimens and ensure appropriate case management.
- HSO to ensure the above-mentioned processes are duly undertaken. Where required HSO should assist in case investigation, sample collection and transportation of specimens to designated lab.
- HSO is also responsible to prepare & submit line listing report to CS/CHO, notify DSFP, contact SIMO when necessary.
- Suspected Measles Case Investigation Forms (CIF) will be sent to the National laboratory along with the specimens.
- If there are cases with no laboratory specimens, case investigation forms of those cases also to be sent to the national laboratory.
- NPML will complete the "Status of specimen condition" section of the CIF for each suspected measles case with sample. At national level EPID number is checked and corrected if needed. A copy of CIF with completed specimen condition part for cases with samples and checked and corrected EPID number to be sent to Surveillance and Immunization Medical Officer (SIMO) responsible for the area.
- The SIMO also to be notified to provide technical assistance to ensure proper investigation of cases.
- CS/CHO will compile the information of AFP & EPI Disease Weekly Line listing form coming from each surveillance unit under the catchment area and submit the report to EPI HQ by following Tuesday.

Role and responsibilities of DSFPs/LSOs/SIMOs and National level

Role of Local Surveillance Officer (LSO) and or Surveillance Immunization Medical Officer (SIMO) in Active weekly surveillance

- The assigned officer, usually the LSO along with the SIMO for the particular hospital will visit the hospital every week to review inpatient registers, outpatient registers and logbooks for any suspicious measles/rubella cases.
- S/he will contact pediatricians, neurologists, medical officers and nurses to determine if any new suspected cases of measles/rubella were identified during the previous week (since last visit to current visit)
- The visit to be documented by signing the registers/records that are checked
- The LSO and/ or SIMO will complete the AFP, NT, Measles and CRS Weekly Active Surveillance form and submit to EPI/HQ by Tuesday of the following week
- Ensure case investigation forms for suspected measles/rubella are send to the national laboratory along with the specimens as appropriate collected

SIMO encourage reporting of suspected measles cases, facilitate timely reporting to CS, CHO, facilitate case investigation, collection of specimens and case management.

Role of UH & FPO/MMO/ZMO/AHO at Upazila/Zone/Municipality level

- Prepare line listing report (AFP& EPI Disease Weekly Line listing Form for hospitals and upazila health complexes) and send to the Civil Surgeon office or the City Cooperation CHO office by next Tuesday, even if no cases identified, zero reporting)
- Ensure case investigation of measles cases using Suspected Measles Case Investigation Form. (Annexure-09)
- Ensure blood specimens, nasopharyngeal swabs/urine are taken from suspected cases and arrange for transport of the specimen to the national laboratory with suspected measles case investigation forms.
- Provide feedback to field staff to initiate control measures

Ensuring that all data from cases are properly collected, analyzed and interpreted for local action.

Role of Civil Surgeon/ Chief Health Officer at the District/City Corporation level

The Civil Surgeon office and the CHO office will compile the data of the health facilities in their area and submit to EPI-HQ.

The following surveillance activities need to be carried out at the district/city corporation level

- Monitoring weekly surveillance reports of measles cases including zero case reports submitted by health facilities and submit to EPI-HQ
- Ensuring weekly analysis of measles cases to identify any suspected outbreaks

- Ensure blood specimen, nasopharyngeal swab or urine specimen are taken from suspected cases and arrange for transport of the specimen to the national laboratory
- Ensure appropriate case management
- In case of suspected outbreak organize outbreak investigation and management through district/city corporation rapid response team
- Ensuring that all data from cases are properly collected, analyzed and interpreted for local action

Monitor timeliness and completeness of weekly reporting.

Role of EPI Manager at National level

- Confirm cases and outbreaks using serology and virus isolation at the National Laboratory
- Analyze disease patterns and trends, interpret surveillance data in conjunction with the routine immunization coverage data and produce routine reports
- Monitor surveillance performance using standard indicators
- Supervise and provide technical support to district and divisional level activities
- Provide feedback to peripheral levels and forward data for action
- Use data to evaluate national objectives and to guide the control programme.

Steps of Case Investigation & CIF filling up

Case investigation is important to confirm the disease and identify the magnitude of public health response required. Medical officer assigned by DSFP should be responsible for case investigation within 48 hours of case reporting. Every reported case is investigated using standard "Suspected Measles Case Investigation Form" *(Annexure 09)* which captures certain core variables like notification/investigation information, case identification, hospitalization, history of vaccination, clinical symptoms, travel, contacts, specimen collection, feedback etc.

Key components for filling up the MR-CIF:

1. Assign MR EPID number (by upazila/CC/Mun health authority), as unique identifier as per SOP given below.
2. Record Type of Case(s): (Sporadic/Outbreak); sporadic are isolated cases that are scattered across the Upazila/Municipality/City Corporation without any clustering/contiguity in place and time and do not fit in to the prescribed outbreak definition. If case belongs to an outbreak, mention outbreak-ID (Ex: MSL BAN-DIS-UPZ/CC/MUN-YR-Outbreak No.).
3. Fill up background information section with date of notification, name and designation of the person notifying, date of investigation, facility name and medical record.
4. Complete case identifications details including name, age, sex, address etc. in the second section.

5. Take clinical information of each reported suspected case for signs and symptoms.
    - Date of onset of rash is the most important date and should be strictly assessed and validated.
    - History of fever with maculopapular (non-vesicular) rash along with cough/coryza/ conjunctivitis/joint pain/lymph node enlargement.
6. Take vaccination history of Measles-Rubella Containing Vaccine (MRCV) in detail in both RI and SIAs
    - Measles vaccine (M/MR/MMR) received through routine EPI (before rash onset) including both doses of MRCV1 and MRCV2 by card/history
    - Measles vaccine (M/MR/MMR) received through SIA campaigns (before rash onset)
    - Total MCV (M/MR/MMR) doses
    - Date of last dose of MCV (before rash onset)
7. Take epidemiologically significant travel history of suspected case, to identify the area/district from where case picked up infection (i.e., within the last 30 days before rash onset) which will help to determine the district of residence based on incubation period and more importantly help in prioritising for the contact tracing/active case search activities.
8. Collect serum sample from all suspected cases within 28 days of rash onset and in addition collect anyone (throat swab/nasopharyngeal swab) samples if the case is investigated within 7 days of rash onset, for both serology and virology respectively.
9. Ensure proper shipment of collected specimens to the designated WHO accredited Measles laboratory network under cold chain along with properly filled Measles-Laboratory request form.
10. Rubella in a pregnant woman: A laboratory confirmed rubella case detected in a pregnant woman needs to be followed up till the outcome of pregnancy for observation and record of foetal outcome for any abortion/stillbirth/congenital anomalies in the new-born like congenital cataract, congenital deafness and congenital heart disease/ any other anomalies suspected in a CRS case (additional tests may be required for the new born; case investigation using standard CIF should be completed for suspected CRS).
11. Record Final classification based on laboratory result and in case of nil/inadequate sample, clinical case classification may be done.

EPID number (unique case ID)

- It is critical to assign a unique case identification number to each suspected case. This case identification number should begin with one or more three-letter combinations to designate the geographic location, followed by the year and the case number. Forms, specimen labels and all communications related to the case should cite the unique case identification number. The box below gives an example of a unique case identification number.
- It is a 16-character alphanumeric figure given as a unique case identifier.

- First 3 charters signify disease (MSL), next 3 characters for country code (BAN), next 2 for district code, next 3 character for Upazila/City Corporation/Municipality code, next 2 for year of rash onset and next 3 is the serial no. of the cases in that year in the same upazila/City Corporation/Municipality.
- Any error in the EPID no. may misclassify the cases/outbreaks.

For Sporadic Cases

MSL BAN-33-286-22-001

MSL: indicate disease Suspected Measles

BAN: country code

33: district code (Khulna)

286: Upazila Code (Koyra)

22: year of rash onset

001: serial no. of the cases in that year in the same Upazila

3.3.7 Laboratory diagnosis

Clinical diagnosis is not sufficient to confirm measles infection. The most common test used to confirm measles diagnosis is the presence of measles-specific IgM antibodies in sera collected from suspected measles cases. Isolation of measles virus is extremely important for molecular epidemiologic surveillance to help to determine the geographic origin of the virus and the virus strain circulating in the country.

The ELISA test for detection of measles-specific IgM antibodies: Measles-specific IgM antibody appears within the first few days of onset of rash, attains peak level approximately one week later, decline rapidly after one month and rarely detectable at six weeks after rash onset. In the first 3 days after rash onset test for IgM may give false negative result in 20% cases. The detection of measles IgM antibody in the blood of a clinical measles case can be considered confirmation of measles virus infection.

IgM is also produced on primary vaccination and it may decline more rapidly than IgM produced in response to the wild virus. Vaccine and wild virus IgM cannot be distinguished by serological tests. A vaccination history is therefore essential for interpretation of test results.

Virus isolation/detection: Nasopharyngeal swab and urine specimen are used for Isolation of measles virus in cell cultures. Nasopharyngeal swab and urine sample for virus isolation to be collected within 7 days of rash onset. The detection or isolation of measles virus in clinical specimens can also be used to confirm measles diagnosis. This provides very important information about geographic origin of measles virus importations and complements information obtained from epidemiologic investigation. In addition, when vaccine related cases are investigated, sequencing of a viral isolate allows discriminating between vaccine and wild-type strains.

3.3.7.1 Specimen collection and transportation

Whenever measles/rubella is suspected, designated personnel should secure specimens for laboratory confirmation.

Samples required for measles surveillance:

- Serum
- Throat swab
- Urine

Adequate blood sample should be collected on first contact with the patient during the case investigation. It is also recommended to take the nasopharyngeal swab/throat swab for virology along with the serology specimen by 7 days of rash onset. The likelihood of detecting IgM antibodies is high if blood specimen is collected between 3 and 28 days after onset of rash. Shipment of the sample to a recognized laboratory should take place as soon as possible, maintaining appropriate cold chain (4–8°C).

Venous blood collection for serology

- Venepuncture in sterile labelled tube (5 mL for older children and adults and 1 mL for infants and younger children).
- Whole blood can be stored at 4–8°C for up to 24 hours before the serum is separated.
- Whole blood should be allowed to clot and then centrifuged at 1000 × g for 10 minutes to separate the serum.
- The serum should be carefully removed with a fine-bore pipette to avoid extracting red cells and transferred aseptically to a sterile labelled vial.
- Serum should be stored at 4–8°C until shipment takes place, but not more than a maximum of 5 days. When kept for longer periods, serum samples must be frozen at temperature of –20°C.

Serum Collection procedure

A single blood specimen should be collected from each case at the first contact within 28 days of onset of rash.

Collection-kit

- Lab request form
- Cryovial, 5ml sterile blood collection tubes
- Cryovial, 2ml sterile serum storage vials

- Tourniquet
- Specimen label for cryovials, marker pen
- 5 ml syringe with 23G needle
- Butterfly/scalp vein with 23G needle
- Band aid
- Disposable gloves and face mask (one set each)
- Alcohol swab
- Gauge pieces
- Zip lock plastic bags
- Plastic dropper
- Hub cutter
- Vaccine carrier with four ice packs

Blood - Serum Collection Kit

- First aid kit (Along with address of nearest referral facility in case of blood clotting complications)
- Waste disposal bag.

Collection method

- Explain the subject/parents about blood collection.
- Determine the best collection site (e.g., wrist, cubital area).
- Clean your hands with the hand sanitizer and put on a new pair of disposable gloves.
- Tie a tourniquet proximal to the site of puncture.
- Clean the venipuncture site as follows:
  - o Wipe with an alcohol swab using a circular motion from the centre to the periphery
  - o Allow the area to dry for at least 30 seconds
- Collect 5ml blood by venipuncture in a sterile cryovial labelled with patient identification and collection date.
- Release the tourniquet and press the puncture site with sterile gauze for about 15 seconds until the blood oozing stops. Then apply a band-aid at the site of puncture.
- The blood should be kept at room temperature for at least 45 minutes to allow clot formation.

- After this time, place the cryovial containing blood in the vaccine carrier with **conditioned ice packs** and keep it at 4–8^{0}C until transportation to centrifugation site.
- Fix the cryovial in the rack and immobilize the rack inside the vaccine carriers with proper packing (carton sheets, paper) to prevent shaking/hemolysis during transportation.
- Blood can be stored at 4-8°C for up to 24 hrs. before the serum is separated.
- Do not freeze whole blood.
- There are three options available to ensure that the proper specimen reaches the WHO accredited measles-rubella network laboratory.
    - Option 1: Transport whole clotted blood specimen to laboratory in ice, if it can reach the laboratory within 24 hours.
    - Option 2: Whole blood should be centrifuged at 3000 rpm for 10 minutes to separate the serum and then collect the serum in separate tubes and transport.
    - Option 3: If centrifuge is not available, carefully remove the serum following complete clot retraction after holding over blood samples overnight in 4-8^{0}C in cold chain using a pipette/dropper supplied to avoid extracting/mix-up of red cells.
- Transfer the serum aseptically to a sterile externally threaded 2ml cryovial, with case ID and other details.
- Store the serum at 4-8°C until shipment takes place.

Shipment

- Specimens should be shipped to the designated laboratory as soon as possible (preferably within 48-72 hours of collection) in cold chain. Do not wait to collect additional specimens before shipping.
- Place specimens in Zip lock or plastic bags.
- Place lab- request form inside plastic bag.
- When the arrangements have been finalized, inform the lab of the time and manner of transportation.

Remember

- Label the vial with the patient's name, EPID number, specimen number for outbreak.
- Fill in Measles Rubella Lab Request Forms (MR-LRF) completely.
- Three important dates:
    - Date of onset of rash
    - Date of last measles vaccination
    - Date of collection of sample
- Sterile serum should be shipped in vaccine carrier with conditioned ice pack within 48 - 72 hours of its collection.
- In rare scenario sterile serum can be stored at 4-8°C for a maximum period of 7 days or in case a delay of more than 7 days is anticipated, sera must be frozen at -20°C which needs to be transported to the WHO accredited laboratory in frozen condition.

Repeated freezing and thawing can have detrimental effects on the stability of IgM antibodies.

Alternate specimen collection for serology

Dried blood spot collection

- Skin punctures the finger or heel using sterile lancet (for young children before they start to walk).

Up to four full-circles of whole blood are collected on standardized filter paper. One to two drops are collected to completely fill each circle of a filter paper (whatman protein saver) properly labelled for each case. (1st circle for Measles IgM, 2nd circle for Rubella IgM, 3rd circle for repeat test if required, 4th circle for quality assurance processes in the lab).

- Allow the filter paper to dry thoroughly before enclosing in a plastic bag or envelope.
- Samples do not need to be kept refrigerated or frozen during transport; it is advisable to store in a cool place and transport to the laboratory as soon as possible, preferably within 5 days.
- Thoroughly dried blood spot samples are no longer subject to IATA (International Air Transport Association) dangerous goods regulations.

Oral fluid collection

- Use a special swab (such as a toothbrush) to collect crevicular fluid from the gum area of the mouth. The swab should be rubbed along the gum for around 1 minute until the device is thoroughly wet.
- Place the wet swab inside a clear plastic tube available for the purpose and label it.
- Ship samples within 48 hours to the lab. If the daily ambient temperature is below 22°C, samples should be shipped to the laboratory within 24 hours. At higher temperatures, samples should be kept in a refrigerator until shipping to the laboratory on ice.
- The samples are usually not considered biohazardous and can be shipped without special documentation from the site of collection to the laboratory.
- Specific instructions provided by the device manufacturer should be followed.

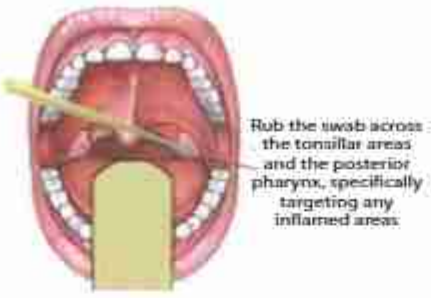
Virology

Data on viral genotypes are critical for identifying the source of cases whether they are indigenous or imported and the place of origin if imported (when number of cases have come down drastically). Therefore, specimens for viral detection and isolation should also be collected on first contact with the patient for every case and in large outbreaks for 5–10 cases.

Throat/Nasopharyngeal swab samples for virology

Anyone (throat/Nasopharyngeal swab) will be collected from each suspected MR case within 5 days of onset of rash.

Throat swab collection procedure and collection kits



Kits required

- VTM (viral transport media)
- Sterile swab
- Tongue depressor
- Sticker labels
- Mask and gloves.

Collection Method

- For throat-swab ask patient to open mouth and use tongue depressor then with the use of sterile swab rub the surface across the tonsillar areas and posterior pharynx, specifically targeting any inflamed areas.
- Nasopharyngeal swabs are obtained by rubbing the nasopharyngeal passage through inserting the sterile swabs to dislodge epithelial cells.
- The swab collected are then placed in labelled screw-capped tubes containing sterile VTM and kept in cold chain.

Shipment

Specimens collected should be transported to the designated Measles laboratory after proper labelling of VTM tubes with EPID No. and completed Measles CIF and Laboratory Request Form (LRF) at the earliest as possible.

Alternate specimen collection for virology

a. **Urine sample** - the measles virus is present in acute cases of measles in the cells that have been sloughed off in the urinary tract. Urine is collected for virology if throat swab is difficult to obtain. It is preferable to obtain the first urine passed in the morning.

- About 10–50 ml of urine should be collected in a sterile container and held at 4 to 8 °C before centrifugation.
- The virus is concentrated by centrifugation of the urine and the cell pellet re-suspended in a suitable viral transport medium.
- Urine must NOT be frozen before the concentration procedure is carried out.
- Whole urine samples may be shipped in well-sealed containers at 4°C, but centrifugation within 24 hours after collection is preferable.

- Centrifugation should be performed at 500xg (approximately 1500 rpm) for 5 to 10 minutes, preferably at 4°C. The supernatant should be discarded and the sediment resuspended in a 2 to 3 ml sterile transport medium, tissue culture medium or phosphate-buffered saline.
- The resuspended pellet may be stored at 4°C and shipped within 48 hours to a measles reference laboratory. Alternatively, it may be frozen at –70°C in a viral transport medium and shipped on dry ice in a well-sealed screw-capped vial.

b. Oral fluid - similar to that described earlier for serology.

Table 4: Summary-sample for laboratory diagnosis of measles and rubella

Type of Specimen	Test type	Volume to collect	Timing for specimen Collection	Storage Conditions
Serum (venepuncture)	Ig M Antibody detection	5 ml of blood; 1 ml for infants and younger children; 0.5 ml from small infants.	≤28 days post rash onset Paired sera are normally collected 14-21 days apart. The interval between the two serum samples can be shorter if virus-specific IgG was not detected in the first serum sample.	4–8°C
Alternative specimen: Dried blood spot 9 DBS)	Ig M Antibody detection Detection of viral RNA by RI-PCR	At least 3 fully filled circles on a filter-paper collection device	≤28 days post rash onset	No cold chain required
Throat, nasal, or nasopharyngeal (NP) swabs or nasopharyhgeal aspirates**	Viral isolation and detection of viral RNA	swab or NP aspirate	Within 7 days after rash onset for viral isolation (cell culture). Up to 14 days post rash onset if performing virus detection using RT-PCR	4–8°C
Oral Fluid (OF)	IgM antibody detection IgG antibody detection Detection of viral RNA by RT-PCR	Using a sponge collection device to collect ~0.5mL crevicular fluid).	Up to 14 days post rash onset if performing virus detection using RT-PCR up to 28 days if antibody testing	Does not require cold chain if <22°C ambient temperature
Urine	Viral isolation by cell culture Detection of viral RNA by RT-PCR	Minimum 10 ml (preference first morning void). Larger volume with higher chance of detection	within 5 days after rash onset	Spin down cell pellet and re-suspend in buffer for storage and transport at 4-8°C

3.3.8 Case management

Children with mild illness may preferably be managed at home without compromising on access to health care and avoiding contact with other vulnerable children. Seriously ill children should preferably be hospitalized for proper management. Since the measles virus is highly infectious, all hospitalized children with suspected measles should be cared for in an isolation facility. School-aged children and working adults should avoid public places and remain confined at home for at least 5 days after the onset of the rashes. There is currently no specific antiviral treatment for measles or rubella. Administration of vitamin A to children with measles has been shown to decrease both the severity of disease and the case-fatality rate, and WHO recommends that vitamin A be administered to all children with measles: 50,000 I.U. for infants aged less than 6 months, 100,000 I.U. for infants aged 6–11 months and 200,000 I.U. for children aged 12 months of age and older. Administration of vitamin A should be provided at the first health service contact and one dose should be administered the following day. If the child has clinical signs of vitamin A deficiency (such as Bitot's spots), a third dose should be given 4–6 weeks later. For uncomplicated cases, fluids (such as oral rehydration solution), antipyretics and nutritional therapy are commonly indicated. Many children require 4 to 8 weeks to fully recover their pre-measles nutritional status. Treatment should be provided for the cases with complications.

For rubella, care is supportive for non-pregnant persons. For pregnant women with suspected rubella, a comprehensive investigation including laboratory testing should be conducted. Pregnant women with confirmed rubella should be followed till the completion of her pregnancy to document the outcome (i.e., normal, CRS, miscarriage, stillbirth, etc). For those pregnancies that go to delivery, the new-born should be placed in contact isolation and evaluated for suspected CRS.

3.3.9 Treatment

Even though there is no specific treatment for measles, limited studies have demonstrated some clinical benefit of the antiviral drug ribavirin. Administration of vitamin A to children with measles has shown to decrease both the severity of disease and the case fatality rate. Vitamin A is important to support intestinal and respiratory epithelial integrity and prevent post measles pneumonia, severe diarrhoea and blindness. Vitamin A supplementation should always be given to any suspected measles patient. Appropriate treatment of bacterial complications with antibiotics is essential. For uncomplicated cases, fluids, antipyretics and nutritional therapy are commonly indicated. Many children require four to eight weeks to fully recover their pre-measles nutritional status.

Table 5: WHO recommended Vitamin A Schedule for measles treatment

Age	Immediately on Diagnosis	Next Day
<6 months	50,000 IU	50,000 IU
6-11 months	100,000 IU	100,000 IU
12 months and above	200,000 IU	200,000 IU

Vit. A Capsule
(Blue with 50,000 IU & red with 200,000 IU)

Significant note

- Two doses of vitamin A should be given as recommended above.
- Only a properly trained field worker should be allowed to administer vitamin A dose.
- The above schedule is for treatment of measles cases and not for vitamin A prophylaxis.
- In case of severely complicated measles with corneal clouding, a 3rd dose should be given after 14th day.

Vit. A is lifesaving drug in measles outbreak. Each district should ensure adequate stock of Vit. A at upazila/Municipality/CC level

3.3.10 Public health intervention

Public health intervention should be initiated for all confirmed cases of measles or rubella. In measles elimination settings, a single case is considered an outbreak and evokes public health response. The key components of public health response are:

1. Contact Tracing

Conduct contact tracing to identify the source of infection and determine whether other areas have been exposed or are also experiencing outbreaks.

- Identify all people that the case had direct contact during the time s/he was contagious.
  - for measles: 4 days before and until 4 days after the onset of rash
  - for rubella, 7 days before until 7 days after the onset of rash
- make a line-listing of these contacts, including their names and addresses and phone number.
- determine whether they are or were ill.

The following groups and individuals could be considered as contacts during outbreaks:

- household contacts
- schools contacts, including all school employees and students
- workplace contacts
- Health facility: individuals who shared the same room, including waiting room without appropriate protection.

The following actions should be taken to minimize spread.

- Contacts under 15 years without documented evidence of measles vaccination should be vaccinated and the symptoms of measles should be explained to them.
- During the second week after exposure, and at the first sign of possible measles (fever, runny nose, cough or red eyes), the contact should be instructed to stay at home.
- Follow-up should be done to determine if a contact subsequently became ill (possible signs of measles). If so, laboratory specimens should be collected.

The follow up can be done over phone to and from the health workers/1st line supervisors and affected person.

2. Enhanced case-based surveillance and active case searching

In response to confirmed cases of measles or rubella, active case searches should be conducted to detect unreported cases to ensure that all cases are identified and reported. In the community and in schools, active case searches are conducted by asking key people if they know of anyone with fever and rash. This activity can be aided by using pictures of measles/rubella patients with maculopapular rash. Such searches can be conducted in a perimeter of an entire village, cluster of villages, ward of town or entire town, etc. depending upon a local epidemiological assessment mostly within the radius of 100–1,000 metres from the confirmed case. In addition, health facilities should also be included for active case searches. In health facilities, health staff interview and review registration records, discharge diagnoses, hospital charts, etc. should be performed to identify patients with fever and rash illnesses and their final diagnosis. During and following rubella outbreaks, active CRS surveillance should be implemented with special attention to investigation and active follow-up of pregnant women with suspected rash illness in the affected area. Additional measures could include investigation and vaccination of susceptible contacts to reduce the risk of exposure to pregnant women.

3. Isolation of suspected cases:

Children with mild illness may preferably be managed at home without compromising on access to health care and avoiding contact with other vulnerable children. Seriously ill children should preferably be hospitalized for proper management. Since the measles virus is highly infectious, all hospitalized children with suspected measles should be cared for in an isolation facility. School-aged children and working adults should avoid public places and remain confined at home for at least 5 days after the onset of the rashes.

For confirmed rubella infection, emphasis should be placed on preventing exposure of susceptible pregnant women to prevent CRS.

4. Survey of population immunity/gaps:

Review of coverage trend for MRCV1 and MRCV2, review coverage of MCV SIA or other Periodic Intensification of Routine Immunization (PIRI) if any in the area, identify any immunity gaps, focus especially on any hard-to-reach populations.

5. Enhancing population immunity against measles and rubella:

Conduct an ORI or SIA based on epidemiological data. All children who were found to be unimmunized/partially immunized and those who cannot produce immunization cards or records during the community survey should be vaccinated with measles and rubella containing vaccine (MRCV) according to the national recommendation.

3.3.11 Data management and producing report

A well-developed information and feedback system is necessary which provides programme managers at different level with the information they need for taking appropriate actions on identified problems. As rubella surveillance is integrated with measles so. Case investigation forms, data base and reporting are usually done together for both diseases.

3.3.11.1 Data elements

- Demographic information
- Reporting source

- Clinical details
- Vaccination status
- Laboratory methods and results
- Epidemiological information
- contact tracing and
- case classification

3.3.11.2 Data analysis

- Number of suspected and confirmed cases by age, date of onset and geographic area
- Incidence per million population by 12-month period and geographic area
- Age-specific, sex-specific and district-specific incidence rates
- Proportion of confirmed cases by age group and vaccination status
- Measles vaccine status among confirmed and discarded cases by year and geographic area
- Epidemic curve showing cases over time by genotype/named strain
- Proportion of cases by final classification and source
- Maps of cases
- Proportion of complications and death, stratified by age
- Proportion of cases that are preventable
- Data summaries for endemic and imported virus genotype and lineage characterization.

3.3.11.3 Feedback

At the national level EPI programme manager is responsible for producing regular feedback bulletins or newsletters, highlighting any patterns or trends of disease occurrence and describing the possible causes of outbreaks as well as the quality of response following notification. A copy of the Laboratory result reports should be provided to the respective reporting facilities, such as upazilas, municipalities, districts and city corporations as soon as they are available.

3.3.11.4 Surveillance Performance Indicators

1. Surveillance Attribute: Timeliness of reporting

Indicator: Proportion of surveillance units sending measles and rubella reports, including 'zero-reporting' to the national level on time

Target: ≥80%

Calculation: Timeliness of reporting

Surveillance units reporting measles and rubella data to the national level on time / Total number of surveillance units	X 100

2. Surveillance Attribute: Sensitivity

Indicator: Reporting rates of cases discarded as non-measles and non-rubella as a proxy to sensitivity of surveillance

Target: ≥2 per 100 000 population

Calculation:

$$\frac{\text{Total number of discarded non-measles non-rubella cases}}{\text{Total population}} \times 100\,000$$

3. Surveillance Attribute: Representativeness

Indicator: Proportion of second administrative level units reporting at least two non-measles non-rubella cases per 100 000 population

Target: ≥80% of second-level administrative units

Calculation:

$$\frac{\text{Total number of second administrative level units reporting at least two non-measles non-rubella cases per 100 000 population}}{\text{Total number of second administrative level units}} \times 100$$

4. Surveillance Attribute: Timeliness and completeness of investigation (Adequacy of investigation)

Indicator: Proportion of suspected cases with adequate investigation initiated within 48 hours of notification

Target: ≥80%

Calculation:

$$\frac{\text{Total number of cases with adequate investigation within 48 hours of notification}}{\text{Total number of suspected cases}} \times 100$$

Note: Adequate investigation includes collection of all the following data elements from each suspected case of measles or rubella: Name or identifier; place of residence; place of infection; age or date of birth; sex; date of onset of rash; date of specimen collection; measles-rubella vaccination status; date of last measles-rubella containing vaccination; date of notification; date of investigation and travel history.

5. Surveillance Attribute: Specimen collection and testing adequacy (Laboratory confirmation)

Indicator: Proportion of suspected cases with adequate specimen collection for detecting acute measles and rubella infection collected and tested in a proficient laboratory

Target: ≥80% excluding epidemiologically linked cases

Calculation:

$$\frac{\text{Total number of cases in which adequate serum sample is collected and tested in a proficient laboratory}}{\text{Total number of suspected cases}} \times 100$$

Note: Adequate specimens for serology are those collected within 28 days after rash onset that consist of ≥0.5 mL serum or ≥3 fully filled circles of dried blood on a filter-paper, or oral fluid. For oral fluid samples, the sponge-collection device should be rubbed for about 1 minute along the gum until the device is thoroughly wet; epidemiologically linked cases should be excluded from the denominator.

6. Surveillance Attribute: Timeliness of specimen transport

Indicator: Proportion of specimens received at the laboratory within 5 days of collection

Target: ≥80%

Calculation:

$$\frac{\text{Total number of specimens received at laboratory within 5 days of collection}}{\text{Total number of specimens collected}} \times 100$$

7. Surveillance Attribute: Timeliness of laboratory reporting
Indicator: Proportion of results reported by the laboratory within 4 days of specimen receipt
Target: ≥80%

Calculation:

$$\frac{\text{Total number of results reported by laboratory within 4 days of specimen receipt}}{\text{Total number of specimens received}} \times 100$$

8. Surveillance Attribute: Viral detection
Indicator: Proportion of laboratory-confirmed chains of transmission (defined as one or more confirmed measles cases) with specimens adequate for detecting measles virus collected and tested in an accredited laboratory
Target: ≥80%

Calculation:

$$\frac{\text{Total number of laboratory-confirmed cases with specimens adequate for detecting measles virus collected and tested in an accredited laboratory}}{\text{Total number of laboratory-confirmed cases}} \times 100$$

9. Surveillance Attribute: Immunization Coverage
Indicator: MCV1 & MCV2 coverage nationally and by sub-national administrative units

Target: 95% nationally and sub-nationally

Calculation:

$$\frac{\text{Total number of infants who received MCV1 \& MCV2}}{\text{The surviving birth cohort}} \times 100$$

10. Surveillance Attribute: Outbreak Investigation

Indicator: Percentage of suspected measles outbreaks fully investigated

Target: 100%

Calculation:

$$\frac{\text{The number of suspected outbreaks that meet the fully investigated outbreak criteria}}{\text{The total number of suspected outbreaks}} \times 100$$

11. Surveillance Attribute: Virus detection in outbreaks

Indicator: Percentage of suspected outbreaks tested for virus detection

Target: 100%

Calculation:

$$\frac{\text{The number of confirmed outbreaks tested for virus detection}}{\text{The total number of confirmed outbreaks}} \times 100$$

3.4 Measles Outbreak

3.4.1 Introduction

Outbreaks occur when the accumulated number of susceptible individuals is greater than the critical number of susceptible individuals, or epidemic threshold, for a given population to sustain transmission. Since measles is the most transmissible human agent known to date, even very little vaccine failure rates are of immense concern, because the size of the susceptible population can increase over time resulting in periodic outbreaks of measles.

3.4.2 Objectives of outbreak investigations

1. Study the epidemiology of measles and define the population at risk
2. To provide appropriate case management
3. Review the dynamics of measles infection and impact of measles vaccination
4. To suggest ways to improve measles vaccine coverage
5. To reduce morbidity and mortality due to measles as an ultimate goal.

3.4.3 Detection of Outbreak

The term outbreak generally used when the number of cases observed is greater than the number normally expected in the same geographic area for the same period of time. Investigation of outbreaks provides an opportunity to identify high-risk groups, detect changes in measles epidemiology, weaknesses in the routine immunization programme or in the management of measles cases.

Detection of an outbreak depends on the ability to recognize an increase in incidence of measles cases significantly above the number normally expected. This recognition is easier if a routine measles surveillance system collects information on clinical and confirmed cases of measles. with a sensitive surveillance system, analysis of routine reporting of measles cases to district health authority can point to an outbreak.

3.4.4 Measles Outbreak

Suspected Measles outbreak: is defined as an occurrence of 3 or more suspected measles cases in one month in a rural ward/urban mahalla.

Confirmed measles outbreak

A single laboratory-confirmed measles case should trigger an aggressive public health investigation and response in an elimination setting. An outbreak is defined as two or more laboratory-confirmed cases that are temporally related (with dates of rash onset occurring 7–23 days apart) and epidemiologically or virologically linked, or both over a period of 1 month in a rural ward/urban mahalla.

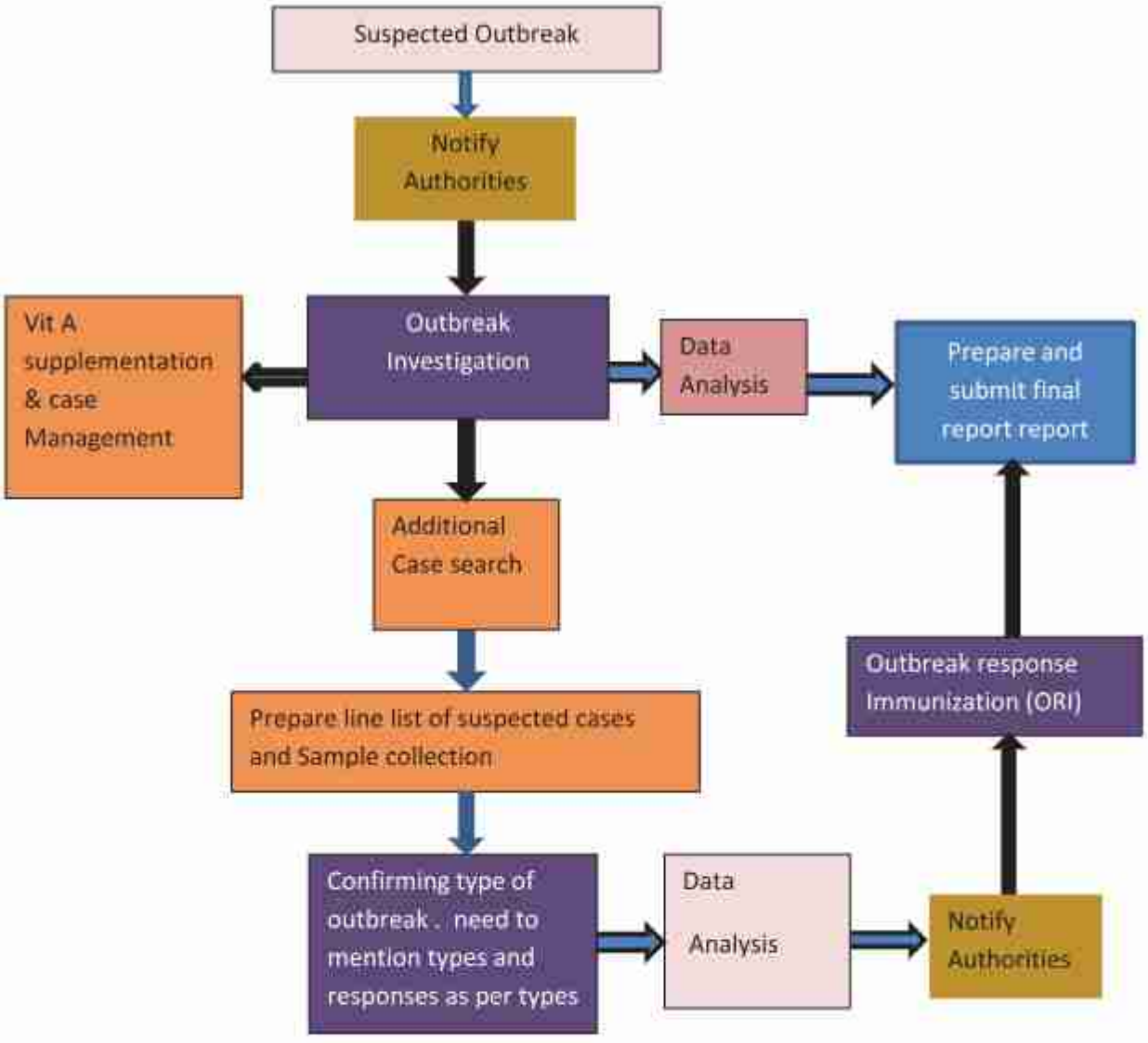
3.4.5 Identification and investigation of outbreaks

Since measles is a very common disease among children, parents often do not seek health care. When complications occur, these cases go to a health facility and reported from there. Therefore, relatively few measles cases are reported through the routine reporting system. However, these reported cases may show the geographical location of outbreaks. When clinically suspected measles cases are reported, it is important to probe from patient or his relatives about the occurrence of similar cases in his surroundings. This helps to detect more cases in the community.

For timely outbreak investigation, it is imperative that routine measles data is collected, collated and analysed regularly by UHFPO/MMO/CHO/CS. Even a single case in a facility may point to an outbreak. Conversations with local health workers may provide more information about an unusual increase in the occurrence of measles in the previous months. Active search should be considered in this situation.

A single laboratory confirmed measles case confirms a measles outbreak during measles elimination. The locality of the suspected measles case should be visited and outbreak control measures and detailed investigation initiated without waiting for laboratory confirmation. Additional cases must be searched. If additional cases are found, then each should be investigated and specimens collected for serology and virus isolation.

3.4.6 Key steps of Outbreak investigation



3.4.6.1 Confirming outbreak

When the data points to an outbreak, the 1st line supervisors (AHI/HI/ FPI/SI/Vaccinator/Supervisor/NGO supervisor/other) should visit the affected area and perform a rapid assessment whether the reported cases are compatible with the case definition of measles/rubella and whether the occurrence of measles/rubella cases has unusually increased or not. Once it is confirmed the UHFPO/MMO/ZMO/CHO/AHO should initiate steps to mobilize the Rapid Response Team and start planning to investigate the outbreak.

3.4.6.2 Organizing outbreak investigation

Once a measles/rubella outbreak is identified in a upazila or municipality or city corporation, it should be investigated in a planned manner. Good planning and homework is the hallmark of high quality of outbreak investigations and produces reliable and accurate epidemiological information. The formation of a Rapid Response Team (RRT) helps in planning, implementation and monitoring of outbreak investigation.

Rapid Response Team (RRT)

Rapid Response team should be mobilized at upazila/municipal/CC level as soon as the outbreak is discovered. The team should consist of the UHFPO/MODC, SIMO/MMO/ZMO/ HO/AHO and MO of Union Sub-center and MA/AHI/HI/EPI-Technician/FW of the affected unions. The RRT should meet frequently to plan and guide outbreak investigation, monitor progress in data collection, compile and analyze data to bring out a final report. The SIMO/ should act as a technical guide to the team.

3.4.6.3 Pre-investigation orientation & planning meeting

The RRT should organize a pre-investigation orientation and planning meeting for medical officers, supervisors and health workers who will participate in the house to house case search and other field activities. The following topics should be discussed in the meeting:

- **Epidemiological investigation**
  - Measles/Rubella/CRS case definition
  - Area affected by outbreak
  - How to conduct case search and house marking
  - Use of forms and formats including method of filling them
  - Supervision of case search and data collection
  - Mapping of measles cases
- **Lab support and Logistics**
  - Lab specimen collection and transportation
  - Logistics and transport facility
- **Case Management**
  - Management of measles cases and referral system
  - Vitamin A doses, schedule, precautions
- **Analysis:**
  - Feedback mechanisms
  - Data analysis and report generation

A map of the Upazila/Union/ Ward showing location of the reported measles cases will help in identifying the affected area and planning the case search. All affected areas should be included in the case search plan. The plan for case search should include day wise allocation of a defined area to each health worker. A map should also be prepared showing the day wise area allocated to each FW. The distribution of work of each FW should be carefully done so that the case search can be performed efficiently. Similarly, each supervisor's area should also be clearly defined.

The families should be sensitized that whenever new measles cases or death due to measles occur, they should report it to the local health worker or nearest health center.

During the course of investigation, some other areas (not included in initial planning) may

report new cases of measles. The RRT should make arrangements to undertake case search in these new areas as well. A practical demonstration of filling out all the forms and formats should be arranged. The procedure of getting the forms back after fieldwork, compilation and transmission of documents should be explained.

Outcomes of the meeting should include:

- Case definition must be cleared to all members involved in OBI
- Action plan for house to house measles case search
- Finalization of man days requirement for data collection
- Finalization of transportation needs
- Finalization of timeline for each activity
- Logistics acquisition and distribution plan
- Basic understanding among health workers and supervisors on case search and data collection
- Fixing job responsibility and monitoring process
- Plan for case management including vitamin A supplementation and referral.

Signs and Symptoms showing complications in measles cases

Case with below symptoms signifies development of complications; should be properly treated and referred to nearest health facility for treatment.

- Unconsciousness
- Inability to feed or drink
- Vomits everything
- Convulsions
- Chest in drawing, stridor
- Diarrhea with severe dehydration
- Ear ache and ear discharge
- Clouding of cornea
- Deep or extensive mouth ulcers
- Severe malnutrition, severe anaemia

3.4.6.4 Planning Logistics

Logistics and supplies should be adequate and timely to support the field investigation. The following items should be arranged and supplied regularly:

- Forms
- Chalk pieces
- Vitamin A Capsules
- Medicines like analgesics, antibiotics, ORS, etc.
- Blood, urine and nasopharyngeal sample collection kit
- Vaccine carrier to transport specimen.

3.4.6.5 Conducting case search

Each worker should conduct house-to-house search to find measles cases in the designated area. All houses should be included in the active case search. The idea is to list all the cases of measles that have occurred in the last 3 months. All measles cases should fit into the standard case definition of measles. Sometimes, an outbreak is detected 2- 3 months or more after the occurrence of the first measles case. Therefore, it will be useful to enquire about measles cases that might have occurred in the past.

The methodology of house-to-house measles case search should be as follows (the health worker should carry ward map, line-listing form for this purpose):

1. Greet the family and explain the purpose of the visit.

2. Enquire from an adult member of the family about the existence of a measles case or occurrence of measles in the recent past (at least 3 as per measles case definition. Also enquire about death due to measles or its complication in recent past. The best way to get this information from family is:

   a. Find any deaths in the past 3 months in the family;

   b. Then ask whether those death cases had any measles before death. Remember, measles may precipitate and cause death months after the disease.

   3. If any suspected measles case is found, fill out suspected measles case investigation form (*Annexure 09*) for each of the case.

   4. Put tally mark about population information of each household in relevant column of the "Outbreak Investigation: Measles Case Search" form *(Annexure 10).*

   5. Put a spot for each case on the map.

   6. All identified suspected measles cases should be given the first dose of vitamin A as per the policy/dosage guidelines. Explain the purpose of Vitamin A to the family.

   7. Ask the family to report occurrence of new measles cases immediately, if any, in future to local health worker or nearest health center.

   8. Mark the house with chalk. This will tell us which house has not been visited. An example of house marking that could be used is:

M
Date

   9. Case/s with symptoms of complications should be referred to nearest health facility and also should be notified to 1st line supervisor.

   10. Collect vaccination history of MR (Measles rubella) vaccine and prepare line list of unvaccinated/partially vaccinated children of 9 months - 14 years.

   11. Move to the next house and repeat the same process.

   12. At the end of the day, forms should be handed over to 1st line supervisor.

Role of Supervisor

Supervisors have a very important role in ensuring the high quality of case search. They should ensure

- Houses are randomly checked for quality of work
- All areas are searched as per plan and no house is missed/ skipped by health workers
- Adequate supplies are available
- In case of difficulty faced by health worker, provide hands-on help and support
- Provide referral support to measles cases with complication
- Collect forms with spot map at the end of the day
- First dose of vitamin A is to be given to all cases of measles
- Second dose of vitamin A is to be given to all identified measles cases on next day
- Line list of 'zero'/partially vaccinated children (9 months-14 years) to be ensured
- Progress is to be monitored
- Daily feedback to RRT is to be provided

The progress of the house-to-house case search should be monitored regularly by the RRT. They should make certain that data from all areas is received.

3.4.6.6 Specimens Collection in an outbreak

Laboratory specimens should be collected from approximately 5 suspected cases in an outbreak. However, for getting the genotyping information it is always preferable to collect both serum and throat swab and/or urine samples from same case within recommended time schedule.

Key points of specimen collection

Specimens to be collected from 5 suspected cases (preferably within 5 days of rash onset) to ensure both serology and virology.

Epidemiological linkage should be the primary way that new cases are classified during a confirmed outbreak. However, criteria for epidemiological linkage must be sufficiently strict to provide confidence of a high positive predictive value that the epidemiologically linked case is a true measles case. Criteria for epidemiological linkage include being a known contact, being in the same physical setting as the case during their infectious period (shared enclosed airspace such as at home, school or workplace).

In elimination settings, as well as where possible in endemic settings, it is no longer recommended that all cases in a given district/area in a month all be categorized as epidemiologically linked. It is preferable to do better investigations to understand potential relationships between cases. If epidemiological linkage is not established, laboratory testing of the suspected case should be done. After initial confirmation of the outbreak, laboratory testing should be done for suspected cases that arise in new locations or in previously unaffected groups. It is important that the field teams

and the laboratory coordinate their work to make sure laboratory results can be interpreted in the context of the field investigation.

If an outbreak continues over a protracted period, another 5–10 samples should be collected every two months to ensure that the outbreak is still due to measles. Genotyping becomes particularly important when the duration of an outbreak is approaching 12 months in a country in which measles was previously eliminated, in order to determine whether cases are part of the same outbreak or due to new importations of a different measles virus strain.

RRT will identify 5 suspected measles cases for collecting serum sample preferably coupled with throat swab and/or urine and local manager would ensure collection of blood (within 28 days of rash onset) and nasopharyngeal swab and/or urine specimens (within 5 days of rash onset).

The ELISA test for the detection of measles-specific IgM antibody and virus isolation is Recommended at the National Polio and Measles Laboratory which is a part of the WHO measles laboratory network.

Table 6: Type of Specimen with volume for suspected measles outbreak

Type of specimen	Serum	Alternative specimen: Dried blood spot (/ DBS)	Throat, nasal, or nasopharyngeal (NP) swabs or nasopharyngeal aspirates	Oral Fluid (OF)	Urine
Amount	5 ml of blood; 1 ml for infants (<12 months)	At least 3 fully filled circles on a filter-paper collection device	Swab or NP aspirate	Using a sponge collection device to collect ~0.5 ml crevicular fluid	Minimum 10 ml

3.4.6.7 Follow up

- A follow up visit should be planned for the outbreak after one month/46 days from the date of rash onset of last case and complications and deaths, if any, to be recorded
- Follow up of serologically confirmed Rubella outbreaks during the follow up visit:
    - Collect blood for Rubella IgM of the pregnant mothers who have been exposed
    - Send specimens to the national laboratory with the request form
    - Assure counseling of pregnant mothers and future consequence upon expected child
    - Follow pregnant mothers up to 9 months after outbreak; collect blood from the baby to test rubella infection
    - Start search for CRS cases
    - No need to provide Vitamin A if outbreak is confirmed as rubella.

3.4.6.8 End of the particular outbreak

An outbreak is considered over after there have been no further epidemiologically or virologically linked cases for two incubation periods (46 days) from the date of onset of the last case. A final report to be prepared and submitted to EPI to declare the outbreak ended formally.

3.4.7 Classification of outbreak

Outbreaks need to be classified as either measles outbreak, rubella outbreak or a mixed outbreak.

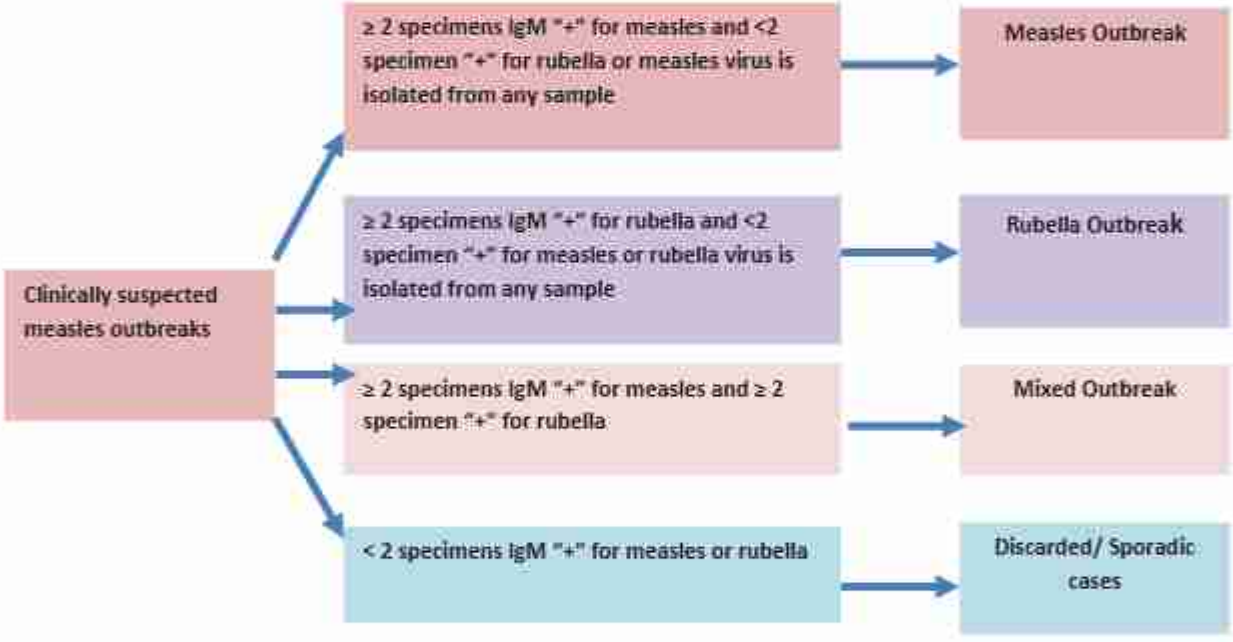
Measles outbreak: If two or more specimens are positive for measles IgM and less than two specimens positive for rubella IgM, or measles virus is isolated/detected from any sample.

Rubella outbreak: If two or more specimens are positive for rubella IgM and less than two specimens positive for measles IgM or rubella virus is isolated/detected from any sample.

Mixed Measles and Rubella Outbreak: If two or more specimens are positive for measles IgM and two or more specimens are positive for rubella IgM.

Discarded/sporadic case: If less than two samples are positive for measles or rubella IgM.

Figure 17: Classification of Clinically suspected measles outbreak



3.4.8 Data compilation and data entry

All forms that are received should be compiled, checked for consistency and entered into computer and analyzed. EPID number to each outbreak will be applied using national coding system.

Data analysis

Data should be analyzed rapidly and locally by the RRT to determine the extent of outbreak, identify groups at risk and evaluate the effectiveness of the routine immunization. Basic analysis

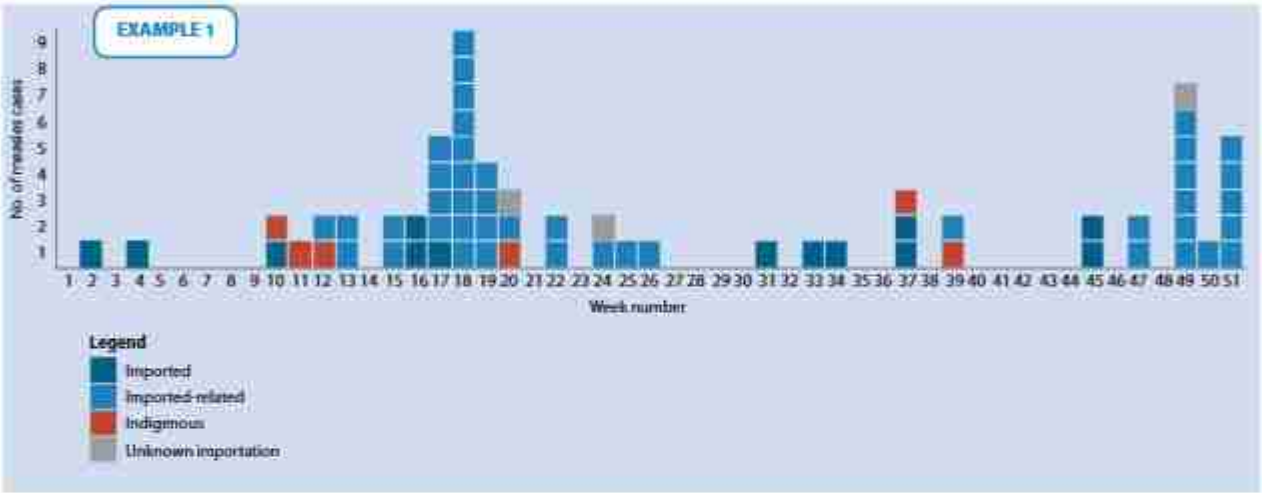
should include preparation of epidemic curve, graph/histogram showing age distribution, vaccination status of cases, spot mapping of cases, age specific attack rates, estimation of vaccine efficacy and proportion of cases that were vaccine preventable.

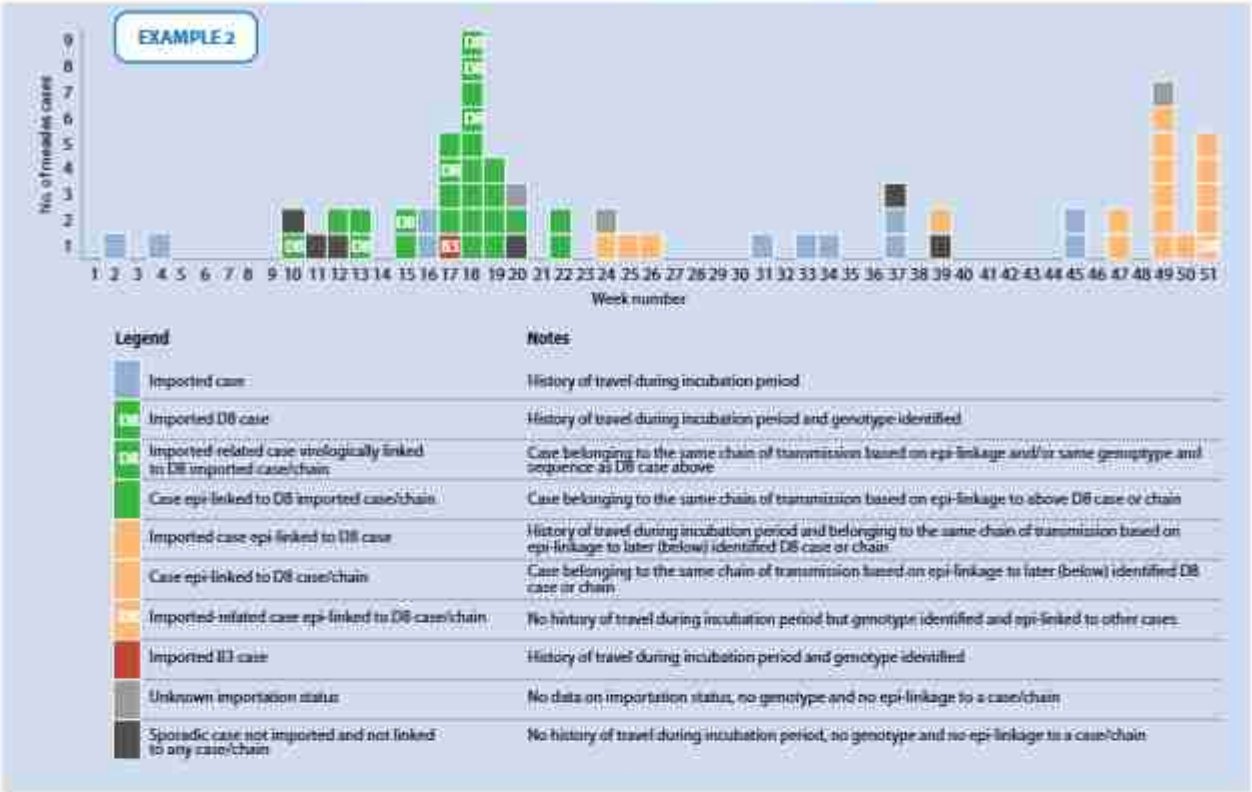
Define the extent of the outbreak (time, place, person)

Time

When did the measles cases occur? An epidemic curve will give that answer. A histogram of incidence of measles cases by week should be prepared. The epidemic curve will show beginning, end, duration and the peak of the outbreak.

Figure 18: Example of an epidemic curve of measles outbreak by source, week of onset, and genotype





Place

Where did the cases occur? A spot map should be prepared showing the actual location of the measles cases. A upazila map showing union boundaries may be used. Individual union maps and urban ward maps may be used to show the outbreak area in greater detail.

Figure 19: Spot map of measles cases

Person

Who is affected by the outbreak? Analysis of the age distribution of cases will show us who was affected by measles in this outbreak - infants, teenage children or adults.

Similarly, a graph of the age and the vaccination status will highlight whether they were immunized or not.

Figure 20: Age distribution of measles cases

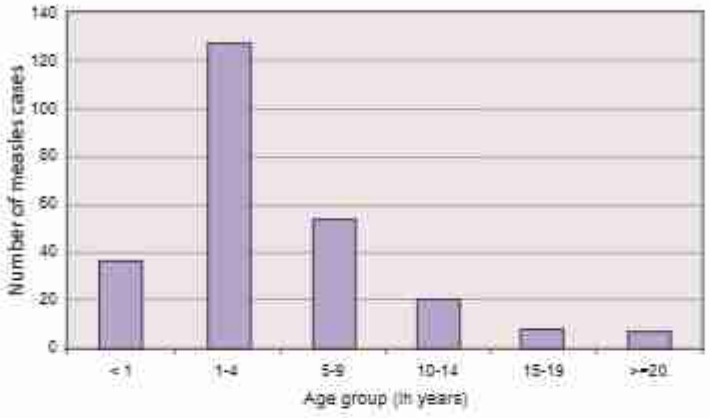
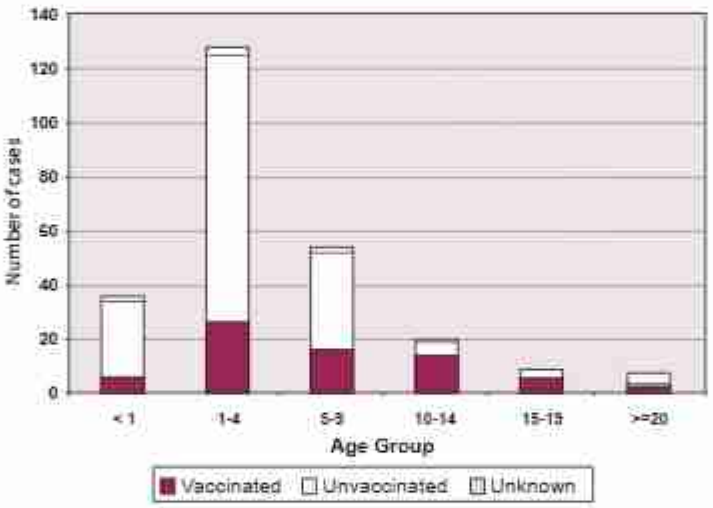


Figure 21: Vaccination status of children



Vaccination Status

Analysis of vaccination status in each age group should be performed to know how many cases could have been prevented by vaccination and how many were not i.e. occurrence of measles before the scheduled age of vaccination. This will also help target subsequent immunization activities.

Age Specific Attack Rates (AR)

Age specific attack rates can be calculated for each age group. For example, the attack rate for age group 1-4 years is calculated as follows:

$$Attack\ Rate\ in\ 1\text{-}4\ year\ age\ group = \frac{Number\ of\ measles\ cases\ in\ 1-4\ year\ age\ group}{Total\ number\ of\ children\ in\ 1-4\ year\ age\ groupx} x100$$

The AR expresses the risk of diseases in population in a given area; The age specific attack rate helps the decision maker to identify priority groups for vaccination.

Table 7: Example of age specific attack rate

Age group	Population	Measles cases	Age specific attack rate
<06 months	25	0	0
06-09 months	10	0	0
09 months to < 1 year	58	13	22
1-4 years	512	279	54
5-9 years	628	290	46
10-14 years	447	158	45
15-19 years	429	22	5
≥20 years	2467	9	<1
Total	4542	771	17

Case Fatality Rate (CFR)

This rate can be calculated as follows:

$$Case\ Fatality\ rate = \frac{Total\ number\ of\ deaths\ due\ to\ measles}{Total\ number\ of\ measles\ cases} \times 100$$

Similarly, the case fatality rate can also be calculated for each age group. Case fatality rate calculation immediately during outbreak investigation may not be accurate. A follow up visit should be planned for the cases after one month from the date of onset of last case. Complications and deaths should be recorded for calculation.

Vaccine Efficacy (VE)

Vaccine efficacy can be determined on the basis of difference between the attack rates among vaccinated persons (ARV) as compared to attack rate among the unvaccinated (ARU), which is expressed as fraction of the attack rate among the unvaccinated group (ARU).

$$Vaccine\ efficacy\ (VE) = \frac{ARU - ARV}{ARU} \times 100$$

The vaccine efficacy can also be calculated by another method when population measles vaccination coverage data is known.

Proportion of vaccine preventable cases (PVPC)

From the data collected it is possible to calculate the proportion of vaccine preventable cases. Vaccine preventable cases are a total of:

- Measles cases who were not immunized

- Measles cases who were immunized before recommended age and not further re-immunized at correct age

$$PVPC = \frac{Number\ of\ vaccine\ preventable\ case}{Total\ number\ of\ measles\ cases} \times 100$$

VE through Case Control Study

Vaccine Efficacy calculation through case control study is not routinely recommended, only in case of measles outbreak where relatively more cases with history of vaccination are detected a case control study may be done. Both cases and controls are recommended to be in the age group of 1-4 years, number of controls should be as much as 4 times the number of cases.

Identifying reasons of outbreak

The analyzed data can determine why the outbreak has occurred. The data will help to identify in which age group the susceptible individuals have accumulated. This will allow corrective measures to be taken.

The analyzed data may show one of the following trends that should point to the reasons of the outbreak:

- High proportion of unvaccinated cases: poor vaccination coverage.
- High proportion of vaccinated cases: high vaccination coverage. Because one dose of measles vaccine does not provide immunity to 100% recipients; it can be expected that cases will occur among some of the individuals who have received only a single dose. However, if there are high proportion of cases in age groups that have received second opportunity, the coverage data and the effectiveness of the vaccine should be evaluated.
- High proportion of cases among children aged 1-4 years: poor routine immunization coverage.
- High proportion of adult cases: measles contracted by susceptible persons who have never been exposed to measles virus or vaccine, e.g. workers from isolated rural areas who have recently migrated to urban areas.
- High incidence in certain areas: vaccination coverage is poor or surveillance is better than elsewhere in these areas.

The reasons for accumulation of susceptible individuals

1. Failure to give vaccine

Some children were not vaccinated: Failure to administer at least 2 dose of MR vaccine to all children continues to be the main cause of measles mortality and morbidity. A high proportion of unvaccinated cases in an outbreak would suggest that a failure to vaccinate children was a significant factor. Spot maps, demographic information and age-specific attack rates can help to identify reasons for a failure to vaccinate.

High-risk areas and groups can be identified with spot maps showing the location of cases. Maps should be examined for clusters of cases that reveal a failure of the programme to reach a specific geographic area or population subgroup. Spot maps of cases can be compared with those maps showing vaccine coverage levels and other data to identify high-risk areas and focus future activities.

Some individuals were too old to be immunized at the onset of the programme: they were outside the target age group for vaccination when the vaccine was introduced and the vaccination programme reduced the measles incidence to lower levels (thus reducing their chances of acquiring natural immunity)

2. Vaccine failure

When first dose is given at 9 months, vaccine efficacy is estimated to be approximately 85%. If the calculated vaccine efficacy (VE) is below 80% during an outbreak in any setting, immunization and cold chain practices should be examined.

If vaccine efficacy is found to be low across all age groups, it is likely that there has been *a cold chain failure*, or that there was a problem with the original potency of the vaccine (as opposed to inappropriate immunization practices).

Cold chain failure: If the efficacy of the vaccine appears to have been low across all age groups, especially during a specific period of time, the cold chain should be reviewed to ensure that it has been functioning correctly. Factors contributing to a cold chain failure must be identified and rectified.

Vaccine potency problems: The initial potency of the vaccine rarely needs to be reexamined. This is an expensive process and should only be undertaken in special circumstances and when adequate samples of vaccine vials are available (e.g. low vaccine efficacy where cold chain and immunization practices are proven to be excellent and when large quantities of vaccine are in question).

Implementing control and preventive measures

Managing cases and contacts to limit spread

It is important to ensure adequate clinical management of measles cases in order to reduce measles mortality. In addition, the following measures should be implemented:

- Limiting contact to only immediate family members who have been vaccinated or have prior history of measles. In particular, avoid contact with infants or young unimmunized children in the household.
- Suspected cases should not be hospitalized unless they have complications or another condition that require hospitalization, because of the intra-hospital transmission.
- Patients with measles who require hospitalization, if possible, be isolated from onset of prodromal symptoms until 5 days after onset of rash.
- Contact should be limited to Outpatient Departments (e.g. waiting rooms) where there are suspected cases. When feasible separate the waiting areas.

Officials would identify the persons who have had contact with a confirmed measles case and take the following actions to minimize spread:

- Contacts (children between 9 months to 15 years) without evidence of measles vaccination to be vaccinated immediately and the symptoms of measles should be clarified to them.
- During the second week after exposure, at the first sign of possible measles (fever, runny nose, cough or red eyes) the contact should be instructed to stay at home (e.g. prevent them from attending school, work, large gatherings).

Appropriate vaccination activities

The RRT and the Surveillance and Immunization Medical Officer (SIMO) investigate the outbreak and are responsible for informing the district level officers (CS/CHO) and EPI/HQ. EPI/HQ will determine the appropriate vaccination activities. Soon after the outbreak is confirmed, the outbreak response team (RRT and the district level officers) should review the risk assessment results and inform the EPI HQ to decide whether to conduct selective or non-selective vaccination activities.

High risk areas and groups can be identified with spot maps showing the location of the cases. Maps should be examined for clusters of cases that reveal a failure of the programme to reach a specific geographic area or population subgroup. Spot maps of cases can be compared with those including coverage levels and other surveillance data to identify high-risk areas and focus future activities.

Step a: Vaccination activities:

As soon as a measles outbreak is suspected, following steps should be taken:

- Enhance social mobilization activities to inform the affected communities about the suspected outbreak, which specific age-group of previously unvaccinated children is targeted for measles vaccination and where parents should bring their at-risk children for vaccination.
- Vaccinate the children (6 months to 14 years of age) as per the information of "line list of unvaccinated/partially vaccinated children' presenting to a health facility or an outreach vaccination site. Based on the data analysis if it is found vaccination failure (poor coverage in the affected area) or vaccine failure, after discussion with EPI vaccination should be done to all children of 6 months to 14 years of age irrespective of history of measles vaccination (either written or verbal). Children receiving measles vaccine before the age of 9 months must be revaccinated after the age of 9 months (one-month interval between 2 doses)·
    - Ensure sufficient supplies: Use stock management records to determine available quantity and location of vaccine, AD syringes and other supplies (e.g. cold chain equipment, Vitamin A, ORS etc.) that are immediately available for use. Estimate and request the additional supplies needed so that activities are not interrupted due to supply stock outs

Step b: Reinforcement of routine vaccination:

A measles outbreak provides an opportunity to identify area/s of weakness of the programme facilitating the outbreak and a chance to take corrective measure. As soon as a measles outbreak is suspected, without waiting for the laboratory confirmation of the suspected measles cases, the following steps to re-enforce routine vaccination should be taken:

- District level staff, Upazila health staff and field staff should rapidly identify priority areas within the district affected (e.g. communities with low vaccination coverage and high risk of morbidity and mortality)
- Jointly work for improving the available local immunization workplan
- Locate health centers organizing immunization sessions that might need additional support for vaccinators and logistics supply
- Adopt corrective measures such as additional outreach services to communities with a high proportion of unreached children.

Assessing the risk of a large outbreak with high morbidity and mortality

As soon as the outbreak is identified, the risk of morbidity and mortality must be assessed. This assessment is needed to determine what type of response is most appropriate to control the outbreak rapidly. For such an action, following evaluation should be carried out:

1. Evaluate the susceptibility of the population and the potential for spread of measles in the affected and neighboring areas.

Approximately 15% of children vaccinated at 9 months of age and 5%–10% of those vaccinated at 12 months of age fail to seroconvert and are thus not protected after vaccination. The example of district X with a population of 500,000 and 12,500 births per year might illustrate to understand buildup of susceptible in a community. If 80% of children aged 1 year receive measles vaccination through routine health services and assuming 85% vaccine effectiveness, only 8500 children (12500 x 0.8 x 0.85) or 68% in each birth cohort will be protected against measles and 4000 children (32%) will remain susceptible to measles. Thus, 4000 children will be added each year to the pool of measles-susceptible children. In general, an outbreak is likely to occur when the pool of susceptible children reaches the size of one birth cohort. In this example, an outbreak is likely to occur in district X after 3-4 years (see table).

Table 8: An approximation of the building up of susceptible children with each successive cohort over a 4 year period in the example district X

Year	Cumulative no. of live birth	Cumulative no. children protected against measles	Cumulative no. of children susceptible to measles
1	12,500	8,500	4,000
2	25,000	17,000	8,000
3	37,500	25,500	12,000
4	50,000	34,000	16,000

To estimate the susceptibility profile by age group, the proportion of susceptible persons should be calculated by taking into account the estimated population and the vaccination coverage of each age group from 6 months to 15 years of age (both through routine immunization and campaigns) and estimated vaccine efficacy.

2.Evaluate the risk of further transmission, morbidity and mortality

For this evaluation, the following factors should be taken into account:

- Population characteristics such as size, density, movement and setting (e.g. community spread throughout a district or limited spread within a sub-population; resource poor settings)
- Under 5 mortality rates
- Nutritional and Vitamin A status
- HIV prevalence in the population
- Time of the year (considering potential for seasonal outbreak) and plans for any festivals or other social events that would result to increase opportunities for spread.
- Internally displaced populations (e.g. Floods, cyclones, earthquakes)
- Number of cases reported and comparison with data from previous years.
- Access to health services

Non-selective mass vaccination activity

As soon as the outbreak is confirmed and the risk assessment result indicates that there is a high risk of a large measles outbreak, then the capacity to carry out a high-quality large-scale immunization campaign should be rapidly evaluated. That is:

- Evaluate the availability of staff and financial resources (both internal and external) for the operational and logistical aspects of the campaign
- Evaluate if the vaccine and other supplies can be made available at the time needed.

If there is sufficient capacity (human and financial resources and vaccine and other supplies) to carry out a safe and timely vaccination campaign, then a mass vaccination campaign should be carried out in the targeted areas (affected and neighboring areas as determined by the risk assessment). However, if the outcome of the assessment does not indicate a mass vaccination response, then selective immunization of unimmunized children presenting to health facilities should be continued and the number of reported cases closely observed and followed to monitor the progression of the outbreak.

For the non-selective mass vaccination response, the timing, target age group and area for vaccination should be defined as outlined below. An accelerated micro-planning exercise should be performed to determine the vaccine, logistics, staffing and communications need for the campaign. Existing country guidelines for conducting mass measles vaccination campaign should be used.

Timing of intervention: Once the decision to intervene is made, it is essential to act quickly to minimize the number of severe measles cases and deaths. If the intervention starts earlier, the impact would be greater. Even late intervention (e.g. immunization) in the epidemic situation, might have role to improve population immunity, shortening the duration of the outbreak and preventing some severe cases and deaths.

Target population: Fixing the target population depends upon susceptibility profile of the population. Key elements to consider in this regard are:

- Routine vaccination coverage and coverage during Supplementary Immunization Activities (SIAs) in each birth cohort
- Age specific attack rates
- Absolute number of cases

It is critical that the results from the outbreak investigation be used to develop and tailor an appropriate and logical response, e.g. to determine additional age and risk groups to target for vaccination. If, for example, the data suggest that older children are affected then the age group initially targeted for vaccination then it should be adjusted to include older cohorts. All age groups contributing to cases should be considered for vaccination. Even if attack rate is low in some age groups, especially in older groups, they may represent a large proportion of cases and large potential group at-risk of both contracting measles and subsequent complications, or in transmitting the infection to younger persons. Once the age group targeted for vaccination is determined, all children in that age group should be vaccinated, regardless of their vaccination status.

Target area: The response should target both outbreak-affected area/s and adjacent area/s in which the risk assessment shows a high risk of spread. As distinct from preventive SIAs (e.g. catch-up and follow-up campaigns) that target entire country, response to outbreak should be more limited in scale.

Health staff should pay particular attention to ensure that groups and areas not being reached and/or at high risk for measles-related complications are reached during routine vaccination activities; and other measures such as the provision of vitamin A should also be provided. These vulnerable groups and areas include:

- young children, particularly those under 1 year of age;
- malnourished and Vitamin A-deficient children;
- infants and children of HIV-infected women and other immuno-compromised children;
- certain ethnic and religious groups who might have poor access to immunization;
- populations with poor access to health care facilities; hospitals and other health facilities;
- all children above 6 months of age who are attending hospitals (inpatients and outpatients) or who are visiting the hospital.

Children receiving measles/MR vaccine before the age of 9 months during a campaign must be revaccinated after the age of 9 months (with one-month interval between 2 doses) since the efficacy of vaccine administered before 9 months of age is likely to be low or strategies to ensure a second dose of MR vaccine include the following:

- inform mothers at the time of vaccination that their child must be vaccinated again;
- notify health workers, NGOs and the community about the need for these infants to receive a second dose.

Target Coverage: Ideally, the target coverage (the proportion of the target population) should be 100%. Once the vaccination activities are conducted, it is important to carry out rapid coverage monitoring to estimate the achieved coverage and to identify potential groups of missed children and ensure they are vaccinated.

3.4.9 Communication and public awareness

When an outbreak occurs, there is likely to be widespread public concern and media attention. In this situation, it is important to keep the public informed and seek their cooperation. The media are useful partners in keeping the public informed through regular message, press releases and conferences. Selecting and using a community spokesperson to act as focal person for the media may be helpful. Messages to the community should be clear and precise using local terminology.

Responsibilities of Rapid Response Team (RRT) after an outbreak

The RRT team should evaluate the following aspects for future endeavor:

- measles surveillance and timeliness of outbreak detection
- cause of the outbreak (example- failure to vaccinate, vaccine failure, etc.)
- preparedness for the measles outbreak
- the management aspect including curative and preventive vaccination intervention
- costs and impact on other health delivery programs
- operational aspect of the immunization programme
- implications for developing appropriate response strategies for future outbreaks! actions.

3.4.10 Writing report

Outbreak investigation should be followed by a short but precise report at the end of the undertaking event. The report should be written systematically including the following sections:

- Introduction/background
- Review of measles/rubella and routine and SIA achievement
- Short review of measles outbreak, if any, in the past

- Outbreak identification and surveillance system
- Specimens collection
- Outbreak Confirmation by serology
- Data collection methodology
- Data analysis
    - Time, place and person
    - Mapping of cases
    - Age distribution and vaccination status of the affected group
    - Attack rate
    - Case fatality rate
    - Vaccine efficacy
    - Proportion of vaccine preventable cases
- Probable reasons of outbreak
- Population at risk
- Case management and vitamin A supplementation
- Response to outbreak
- Conclusions and recommendations
- Future actions
- Enclosure
    - Charts & graphs
    - Maps
    - Key rates and indicators

Report should be sent to District, City Corporation and EPI HQ.

Measles Surveillance and Immunization in acute humanitarian emergency

Measles is a highly infectious disease with grave consequences during humanitarian emergencies, especially those emergencies with displaced populations and among the malnourished. In these settings, the surveillance principle for fever and maculopapular rashes remains the same with all components discussed above. Surveillance system (may need to stablish community based) must be able to identify suspected measles cases with daily reporting for necessary steps. Vaccination during such situation should be based on decision tree as mentioned in WHO guideline "Vaccination in Acute Humanitarian Emergencies: A Framework for Decision Making".

3.4.11 Special activity for measles surveillance

Sero-surveys: High-quality representative sero-surveys can provide ancillary evidence that a country has achieved high population immunity in line with achieving and sustaining measles elimination. The main purpose of conducting sero-surveys in the context of measles and rubella elimination is to identify areas and age cohorts with potential immunity gaps. Serologic testing cannot distinguish between immunity from natural measles infection and vaccine-derived immunity. Sero-surveys should not be used as a substitute for surveillance and can be quite costly and time-consuming to undertake.

3.5 Congenital Rubella Syndrome (CRS)

3.5.1 Introduction

Congenital rubella syndrome (CRS) is the most serious consequence of rubella[22]. Infection with rubella virus is most severe immediately before conception and in early gestation[23]. The virus may affect all organs and cause a variety of congenital defects. Infection may lead to fetal death, spontaneous abortion, premature delivery. The severity of the effects of rubella virus on the fetus depends largely on the time of gestation at which infection occurs. As many as 85-90% of infants infected in the first trimester of pregnancy will be found to be affected if followed after birth. While fetal infection may occur throughout pregnancy, defects are rare when infection occurs after the 20th week of gestation[24]; particularly after 20 weeks of gestation, the fetus can be infected but not develop the signs and symptoms of CRS. These infants are classified as congenital rubella infection (CRI), and also shed rubella virus. Deafness is the most common and often the sole manifestation of congenital rubella infection, especially after the fourth month of gestation. Eye defects, including cataracts, glaucoma, retinopathy, and microphthalmia may occur. Cardiac defects such as patent ductus arteriosus, ventricular septal defect, pulmonic stenosis, and coarctation of the aorta are possible. Neurologic abnormalities including microcephaly and mental retardation and other abnormalities, including bone lesion, splenomegaly, hepatitis and thrombocytopenia with purpura may occur.

Congenital Rubella Syndrome

-Infection may affect all organs

-May lead to fetal death or premature delivery

-Severity of damage to fetus depends on gestational age

-Up to 85% of infants affected if infected during first trimester

Congenital Rubella Syndrome

-Deafness

-Cataracts

-Heart defects

-Microcephaly

-Mental retardation

-Bone alterations

-Liver and spleen damage

Manifestation of CRS may be delayed from 2 to 4 years. Diabetes mellitus appearing in later childhood occurs frequently in children with CRS. In addition, progressive encephalopathy resembling subacute sclerosing panencephalitis has been observed in some older children with CRS. Children with CRS have a higher than expected incidence of autism.

Table 9: Main clinical manifestations of Congenital Rubella Syndrome

Category	Specific manifestation
General	Foetal loss (spontaneous abortion and stillbirth) Low birth weight Mental Retardation
Auditory system	Sensorineural deafness; unilateral or bilateral Central auditory deafness Speech defects
Cardiovascular System	Patent ductus arteriosus Pulmonary stenosis Ventricular septal defects Complex congenital heart disease
Ocular system	Pigmented retinopathy Cataracts: pearly, dense, nuclear 50% bilateral, very often with retinopathy Microphthalmos
Transient neonatal manifestations(extensive infection; high mortality)	Thrombocytopenia with or without purpura Hepatosplenomegaly Meningoencephalitis Bony radiolucencies Adenopathies
Late-emerging or development	Late onset interstitial pneumonitis (age 3-12 months) Insulin-dependent diabetes mellitus

3.5.2 Clinical manifestation of CRS

Hearing loss

Hearing loss occurs in 70% to 90% of CRS cases and in 50% of these children it is the only sign of CRS, although often it is not detected initially. Congenital hearing loss interferes with normal development of speech. Testing for hearing impairment in infants and young children is difficult.

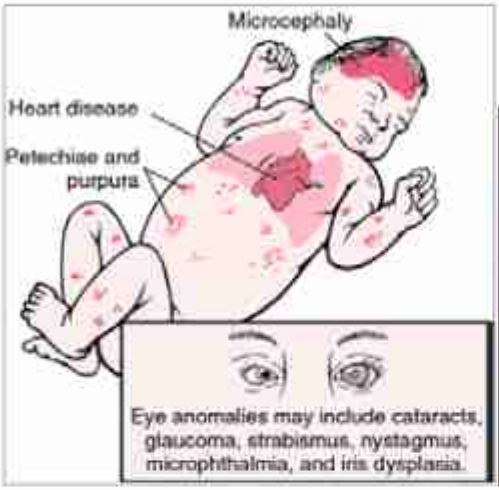
Hearing tests that are used in the developing countries have their advantages and disadvantages. Audiometry in this age group has poor validity and reliability. Distraction test has poor sensitivity and specificity where clinicians/examiners are not well trained. Two newer objective methods used to test infant hearing are: optoacoustic emissions (OAE) and auditory brainstem response (ABR).

Eye signs

Most of the CRS eye signs are readily recognized by parents and health care personnel. Health care worker should suspect CRS, if any of the following eye signs are detected:

- White pupil (cataract)
- Diminished vision
- Pendular movement of the eyes (nystagmus)
- Squint
- Smaller eyeball (microphthalmos)
- Larger eyeball (congenital Glaucoma)

Clinical manifestation of CRS



Congenital Cataract

Immune response in infants with CRS

The serum immune response in CRS differs from that seen in rubella. At birth, the serum of an infant with CRS contains maternally derived rubella specific IgG antibody as well as IgG and IgM antibodies synthesized by the foetus. Maternal rubella specific IgG is also found in normal infants born to women who are immune to rubella. Therefore, rubella specific IgM antibody is used to diagnose congenital rubella infection in infants. In infants with CRS, rubella specific IgM can be detected in nearly 100% cases at age 0-5 months; about 60% at age 6-13 months; and 40% at age 12-18 months. IgM is rarely detected after the age of 18 months.

Infants with CRS shed rubella virus for longer periods. Rubella virus can be found in the nasopharyngeal secretions of more than 80% of infants with CRS during the first month of life, 62% at age of 1-4 months, 33% at age 5-8 months, 11% at age 9-12 months and only 3% during the second year of life.

Infants with CRS who are shedding rubella virus are infectious and appropriate infection control measures should be instituted. It is particularly important to prevent exposure of non-immune pregnant women to these infants.

3.5.3 Laboratory testing for diagnosis of CRS

Collection of 01 ml blood sample preferably using a butterfly needle from every infant, with suspected CRS as soon as after birth is indicated. Almost all infants with CRS will have a positive

rubella specific IgM test in the first six months of life and 60% will be positive during the second six months of life.

3.5.4 CRS surveillance

CRS surveillance allows for detection of infants with clinically apparent manifestations and can be standardized for regional and global reporting, and for comparison. Early identification of infants with CRS is necessary to ensure that appropriate testing can be conducted and that the infant is entered into the CRS surveillance system. Detection of infants with CRS is necessary to ensure infection control and prevent further spread of rubella, as infants with CRS may shed the virus for a prolonged period – up to 1 year of age or longer. Immediate diagnosis of CRS also facilitates early intervention for specific defects.

Year 1996, an estimated 22,000 babies were born with CRS in Africa, an estimated 46 000 in South-East Asia and close to 13,000 in the Western Pacific. The highest risk of CRS is found in countries with high rates of susceptibility to rubella among women of childbearing age

CRS is associated with significant morbidity and mortality. Estimated mortality has ranged from 20–33%. Infants born with cardiac defects have the highest risk of mortality. The South-East Asia Region has the highest burden of CRS cases. The incidence rate of CRS in SEAR is estimated to a mean of 136 per 100,000 live birth since 2008 with a total annual number of CRS cases of 46,621 (95% CI 1016–168 910).

However, the magnitude of rubella and CRS burden in the region remains unknown. In 2010, an estimate 103,000 CRS were born globally, of which 46% were in the SEARO.

CRS surveillance was integrated with AFP and VPDs surveillance in 2012 and 20 cases were reported as clinically confirmed; samples were tested for 18 cases and 2 were laboratory confirmed. The reporting is steadily improving over the time and in 2020 total 175 clinically confirmed and 6 laboratory confirmed cases were reported while in 2021 total 218 clinical cases were reported out of which 10 were laboratory positive.

3.5.4.1 Rationale and objectives of CRS surveillance

Surveillance for CRS compliments rubella surveillance. CRS is the most severe outcome of rubella, and the prevention of CRS is the primary reason for rubella vaccination. The objectives for CRS surveillance are to:

- document the burden of CRS prior to rubella vaccine introduction
- monitor the impact of rubella vaccine introduction in reducing the incidence of CRS
- detect and isolate affected infants rapidly
- mitigate the consequences of the disease for infants and their families through early provision of appropriate medical care
- demonstrate the elimination of CRS.

The key global objective of CRS surveillance is to provide data in support of rubella elimination in five of six WHO regions by 2020.

3.5.4.2 Strategies for CRS elimination

- protection to women in childbearing age through adult immunization
- high routine immunization coverage in childhood to increase population immunity
- large scale supplementary immunization campaign to reduce the circulation of rubella virus
- integrated with case-based measles surveillance and sentinel surveillance for CRS Integrated immunization activities with measles elimination.

3.5.5 Case definition for Congenital Rubella Syndrome (CRS)

Suspected CRS case

Any infant less than one year of age in whom a health worker suspects CRS.

A health worker should suspect CRS when

- there is a maternal history of suspected or confirmed rubella during pregnancy, even when no signs of CRS
- the infant presents with heart disease and/or suspicion of deafness, and /or one or more of the following eye signs: white pupil (cataract); diminished vision; pendular movement of the eyes (nystagmus); squint; smaller eyeball (microphthalmos); larger eyeball (Glaucoma).

Final case classification

Final classification of CRS cases depends, in part, on identifying *Group A* or *Group B* clinical signs of CRS.

Group A: Cataract(s), congenital glaucoma, pigmentary retinopathy, congenital heart disease (most commonly peripheral pulmonary artery stenosis, patent ductus arteriosus or ventricular septal defects), hearing impairment.

Group B: Purpura, splenomegaly, microcephaly, developmental delay, meningoencephalitis, radiolucent bone disease, jaundice that begins within the first 24 hours after birth.

Using these clinical signs, one of the final classifications listed below

Laboratory-confirmed CRS: A suspected CRS case with at least one sign from group A and meets the laboratory criteria for confirmation of CRS

Clinically compatible CRS: A suspected CRS case without an adequate specimen in whom a qualified clinician detects at least two of the complications from group A OR one from group A and one from group B.

Congenital rubella infection (CRI): An infant who has none of the clinical signs of CRS from group A, but who meets the laboratory criteria for CRS.

Discarded: A suspected CRS case with an adequate specimen not meeting the laboratory-confirmed case definition, or a suspected case without an adequate laboratory specimen and not meeting the clinically compatible case definition.

OTHER DEFINITIONS

Based on Source of infection

Endemic CRI/CRS: A confirmed case whose mother was exposed to endemic rubella transmission during gestation, as supported by epidemiological or genotyping evidence. A chain of rubella virus transmission that is continuous for ≥ 12 months within a country is defined as an endemic transmission.

Imported CRI/CRS: A confirmed case whose mother was exposed to rubella outside of the country during gestation, as supported by epidemiological or genotyping evidence.

Unknown source of CRI/CRS: A confirmed case not meeting the above endemic or imported CRI/CRS case definitions.

3.5.6 Case detection and reporting

It is essential to find out the burden of rubella and CRS which requires a comprehensive system to detect suspected CRS cases in infants report them on time.

- Identify rubella cases and/or outbreaks through serological confirmation of all fever and rash outbreaks. Investigate such outbreaks fully and follow them to find out possible increase in the incidence of CRS in the areas
- Conduct sentinel surveillance of CRS at neonatology units, eye hospitals and cardiology units, ENT units and Obstetric units.

Important note

All suspected CRS cases must be investigated by a clinician and with full clinical and laboratory investigation within 48 hours of detection.

The facilities at which infants with most common defects associated with CRS – cataracts, heart defects or deafness as well as infants with maternal history of rubella during pregnancy are likely to be seen and should be included in the CRS surveillance system. As these defects are most likely to be evaluated and treated at secondary and tertiary care facilities, these health-care facilities should be included as reporting sites or sentinel sites at the beginning of CRS surveillance.

The types of facilities/providers most likely to evaluate and treat infants with CRS:

- secondary care providers/facilities, particularly ophthalmologists, cardiologists, audiologists and neonatologists
- tertiary care facilities, particularly those that provide pediatric surgical services for the eyes, ears and heart
- specialty care centers (e.g. children's hospitals; centers for hearing and blindness);
- obstetric centers or private clinics involved in the care of pregnant women with rubella.

As multiple specialties (departments), such as paediatrics, obstetrics, otorhinolaryngology and ophthalmology are involved, a mechanism of coordination between these departments should be developed at the reporting site. One HSO should be responsible for coordination of identifying, investigation, sample collection and reporting. A line list of suspected CRS cases should be

maintained in the assigned facilities. There should be regular communication with the national EPI regarding identification and follow-up of suspected cases of CRS identified in the area.

3.5.7 CRS surveillance in health facilities

CRS surveillance should focus on,

- Identifying infants 0-11 months of age with suspected CRS
- Investigation of all suspected CRS cases by a clinician for clinical confirmation and laboratory testing.
- In implementing CRS surveillance, all active surveillance facilities for AFP and VPD surveillance are to be sensitized to report and investigate any suspected CRS case. The facilities include all district level general hospitals, government and non-government medical college hospitals and some large private hospitals/clinics, specialized hospitals like ICVD, NIO, BSMMU, DSH etc.
- Sites that routinely participate in surveillance for EPI diseases
- Neonatal wards and neonatal intensive care units
- Obstetrics units
- Paediatric wards
- Eye hospitals
- ENT Units
- Cardiology units
- Cardiac surgery units

CRS Surveillance in selected health facilities

- All cases of rubella who meet the surveillance /clinical case definition of rubella when present to the outpatient clinic, emergency room and inpatient ward in health care facilities should be identified and investigated by attending physician. The clinicians (RMOs, MOs, Pediatricians, consultants and other Physicians) of the health care facility collect information from cases at the time they see the patients. They record information on AFP & EPI disease report form and hand over to HSO at the end of their duty.
- The SIMO (surveillance and Immunization Medical Officer) should also be notified if any technical assistance is needed for subsequent investigations including assigning an EPID number to each case.
- The HSO will review the repot forms routinely to ensure that all CRS cases have been investigated and reported to DSFP in the AFP & EPI Disease Weekly Line listing form by following Tuesday.
- Case investigation form (CIF) for CRS (*Annexure 12*) cases will be send to the National laboratory along with the specimens.
- If there are cases with no laboratory specimens, case investigation forms of those cases should also be sent to the National laboratory.
- The National Laboratory will verify assigned EPID number of each case and provide feedback as appropriate.

Active surveillance(weekly) of CRS cases by Local Surveillance Officer (LSO) and/or Surveillance and Immunization Medical Officer (SIMO)

- The assigned officer, usually the LSO along with the SIMO for the particular hospital will visit the hospital every week to review inpatient registers, outpatient registers and clinic records for any possible CRS cases.
- S/he will contact paediatricians, neurologists, medical officers and nurses to find out/ identify if any new cases of CRS detected following the previous visit.
- The visit should be documented by signing the registers/records those are checked.
- The LSO and/or SIMO will complete the AFP, NT, Measles and Rubella Weekly Active Surveillance form and submit to EPI/HQ by Tuesday of the following epidemiologic week
- Ensure sending of case investigation forms for CRS to the national laboratory along with the specimens collected.

3.5.8 Case investigation

When a suspected CRS case is reported, a case investigation form containing core variables should be filled in after clinical evaluation by different departments as per symptoms/signs suspected and sent to the HSO person of the same reporting site for further action. It is critical to note receipt of MR doses through routine service or campaigns (i.e. in children 6 to <12 months) so that laboratory results can be correctly interpreted when classifying cases. *(case investigation form annexure 12)*

Important note

After rubella elimination, a single case of domestically acquired CRS should lead to intensified rubella and CRS surveillance and an investigation to determine where the mother was exposed and the reason for insufficient immunity.

Suspected CRS cases should be investigated within 48 hours of detection. Need to monitor the pregnancy outcomes for pregnant women with suspected or confirmed rubella. For those pregnancies that result in a live birth, ensure that the infant is followed up with appropriate clinical and laboratory evaluation, and placed under droplet and contact precautions to minimize potential spread. After rubella elimination, a single case of domestically acquired CRS should lead to intensified rubella and CRS surveillance and an investigation to determine where the mother was exposed and the reason for insufficient immunity.

Investigation of suspected rubella in a pregnant woman

CRS cases are likely to be underreported where a high proportion of births occur at home and where infant deaths may not be reported. In order to identify CRS cases, it is important to investigate rash illness in pregnant women. If a pregnant woman with suspected rubella infection attending an antenatal clinic, following steps should be followed by UH&FPO/LSO/attending doctor and his/her staff.

- All febrile rash illnesses in pregnancy should be investigated.
- The specimen should be collected and tested for rubella IgM in the National Laboratory. If the blood specimen is positive for rubella-specific IgM, the patient should be counseled

and follow up until nine months.

- All suspected CRS cases aged less than 1 year should be investigated. The investigation should include clinical and laboratory analysis.
- Line listing should be done (AFP& EPI Disease Weekly Line Listing Form for Hospitals and Upazila Health Complexes) and send to the Civil Surgeon office or the City Cooperation CHO office.
- Counseling and medical follow ups should be assured.

Unique identification number

A unique identification number should be given to each investigated case. This unique identification can be alphanumeric (e.g. Disease code + country code + district code + upazila code + year + sequential number by order of reporting), and facilitates further collection and merging of clinical, epidemiological and laboratory data.

Applying standards

Prior to pregnancy & in postpartum period

Vaccinate children, school girl, child bearing age women according to national policy

During pregnancy

Rubella vaccine should not offer

Avoid pregnancy for 1 month after rubella vaccination

Inform to avoid contact with the individual with rubella

Investigate-Suspected rubella in pregnancy, exposure to a rubella case and infants with suspected CRS

Counsel women with confirmed rubella during pregnancy on the risk of fetal abnormalities

3.5.9 Specimen collection and transportation

Efforts should be made to obtain clinical specimens for antibody levels and for viral isolation from infants at the time of the initial investigation. For serological diagnostics, 1 ml sample of blood should be taken and then centrifuged to separate out the serum, which should then be kept under refrigeration at temperatures from 2–8°C. The serum should then be transported in cold chain to the laboratory. Throat swabs should also be collected for isolation of the virus or virus detection.

Laboratory criteria for confirmation of suspected CRS cases include any one of the following:

- rubella IgM antibody over cut-off-point detected
- sustained rubella IgG antibody level as determined on at least two occasions (at least 1 month apart) between 6 and 12 months of age in the absence of receipt of rubella vaccine
- rubella virus detection (e.g. nucleic acid detection by reverse transcription polymerase chain reaction (RT-PCR) or rubella virus isolation) in an appropriate clinical sample (throat swab, nasal swab, blood, urine or cerebrospinal fluid).

Depending on the age of the suspected CRS case at initial testing, the following considerations should be made when interpreting laboratory results and determining final classification of suspected CRS cases.

- Children >9 months may have received rubella-containing vaccine through routine immunization or campaigns and children >6 months may be included in campaigns. Serology results cannot be used to confirm CRS after a child with suspected CRS has received rubella-containing vaccine.

- Infants with congenital rubella will usually be positive for rubella-specific IgM at or shortly after birth. Although IgM antibodies may persist for up to 1 year, they normally peak within the first 6 months of life. Because IgM may not be detectable in some infants tested shortly after birth, IgM negative cases with suspected CRS should be retested at 1 month of age or shortly thereafter.
- Laboratory confirmation of CRS in an infant aged over 6 months should not rely on the IgM test alone if the result is negative. In such cases, serial IgG testing should also be included to check for a sustained level of antibody on two occasions separated by >1-month interval. After confirming IgG+ in the first serum sample collected, this sample should be saved and retested again with the second serum sample to compare antibody levels. If IgM and IgG testing are performed concurrently in ages 6–11 months, any infant testing IgG- should be discarded (all infants with CRS are IgG+).

Infants with congenital rubella should also be tested for shedding rubella virus through virus isolation techniques. Congenitally infected infants may shed and transmit rubella virus for up to 1 year of age and be the source of rubella outbreaks. Therefore, it is important to continue testing the infant for virus throughout the first year of life so that infection control measures can continue until virus shedding stops. This has to be confirmed by two negative results of viral testing of specimens obtained 1 month apart from infants at least 3 months of age.

3.5.10 Case Classification

Case classification will follow an algorithm based on the age of the child, the algorithms are described in Figure below:

Figure 22: Surveillance classification of suspected CRS case-patients < 6 months of age

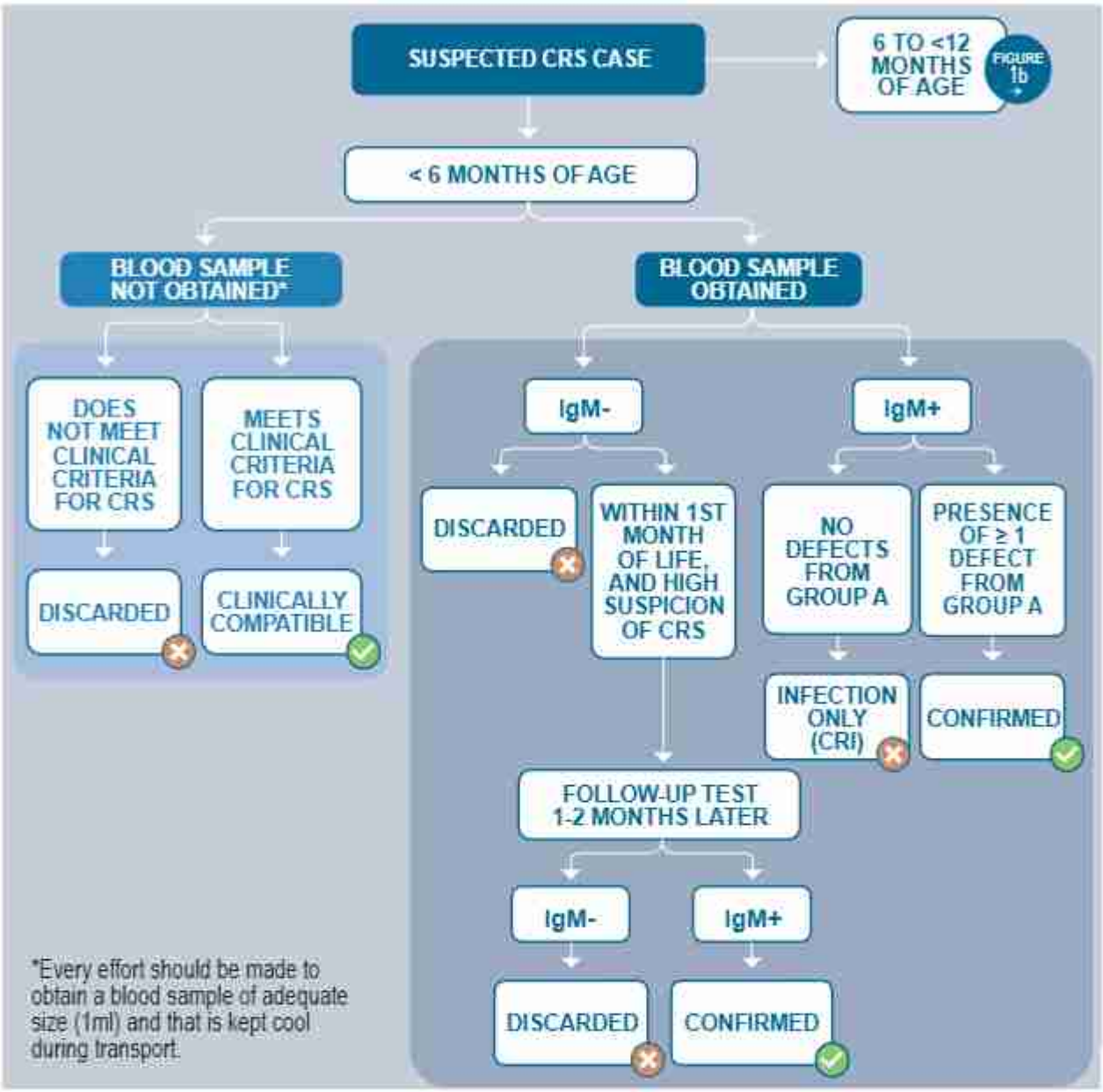
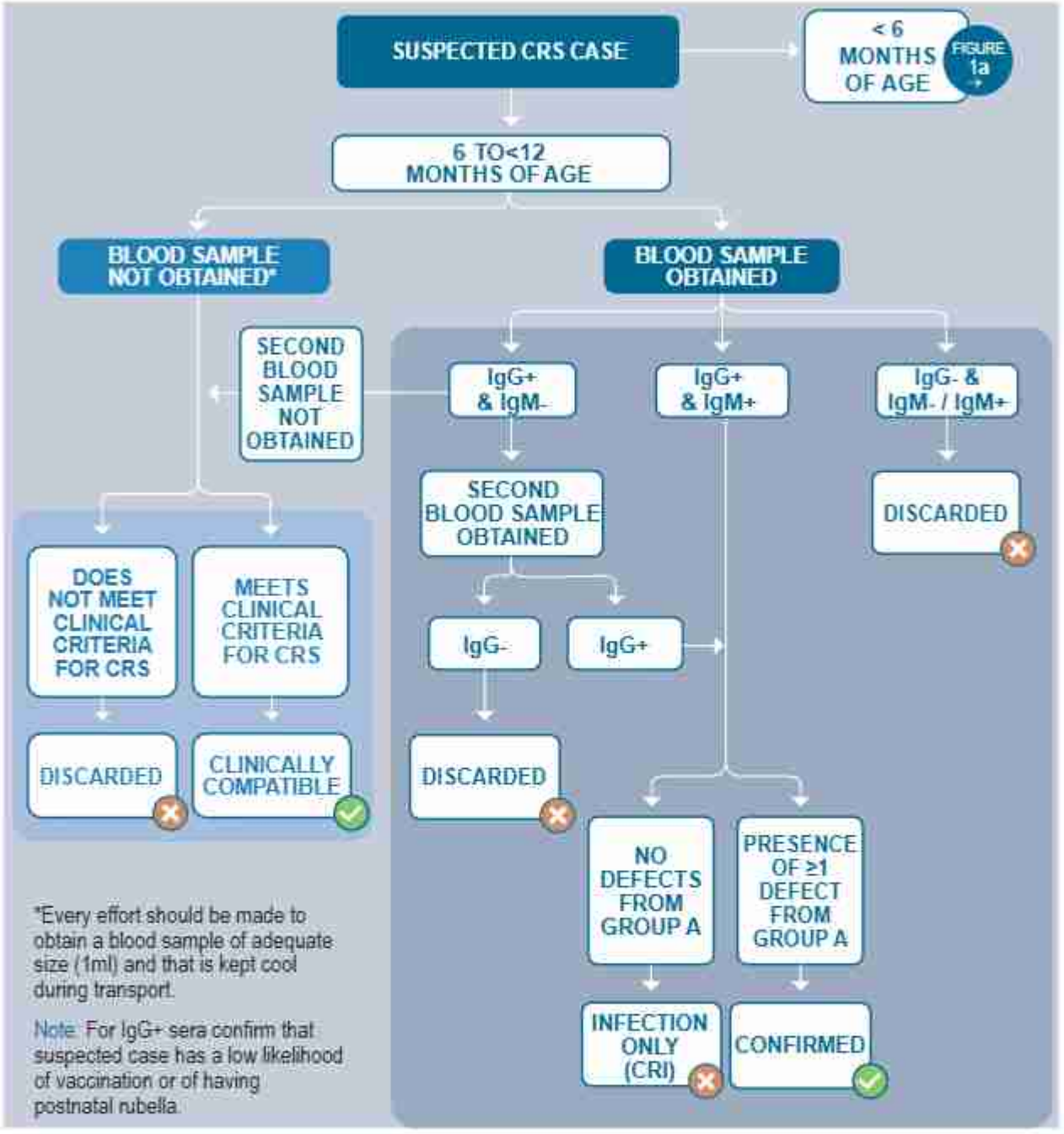


Figure 23: Surveillance classification of suspected CRS case-patients ≥ 6 months to < 12 months of age



3.5.11 Case management

Currently no treatment is available for CRS beyond clinical management of related congenital abnormalities. Infants with CRS and CRI shed live rubella virus for long periods (60% shed for the first four months of life), therefore appropriate infection control measures should be applied.

Important note

Infants with confirmed CRS or CRI should be followed by public health until two consecutive clinical specimens, obtained one month apart, are negative for rubella virus detection/isolation.

In health care settings, contact precautions should be implemented for every detected CRS and CRI case. Infants should be considered infectious until two clinical specimens, obtained one month apart, are negative for rubella virus detection/isolation. Pregnant women should not be exposed to infants with CRS or CRI; if exposed, pregnant contacts should be tested for rubella. In areas where follow-up testing of confirmed CRS and CRI cases is not feasible, emphasis must be placed on ensuring close contacts and health care workers are vaccinated for rubella.

3.5.12 Contact tracing and management

Contact tracing is recommended among mothers of infants with CRS or CRI to identify the source of the rubella virus in the mother. Infants with CRS or CRI shed rubella virus for long periods and appropriate infection control measures should be applied. It is particularly important that pregnant women who are not rubella-immune should not be exposed to infants with CRS or CRI. To prevent further infection with rubella virus and further transmission, protective immunity should be assured among contacts of CRS cases, including health care workers and family members. Persons in contact with the infant should be immune to rubella either through vaccination or natural infection (serological evidence of immunity). Non-pregnant persons who lack documentation of vaccination with RCV can be considered for vaccination. Pregnant contacts should be tested for rubella.

3.5.13 Public health intervention

- Infants with CRS may shed rubella virus for up to 1 year and have been the cause of rubella outbreaks. Only persons' immune to rubella should have contact with these infants.
- In hospitals, infants should remain in isolation.
- Persons caring for the infant should follow universal precautions and should be immunized against rubella.
- Family members and friends involved in the care or handling of the infant based on vaccination history can be considered for vaccination accordingly.
- An active search should be conducted in the community for more CRS cases as well as to review the vaccination status of children in the locality.
- All children in the same locality who are found to be unvaccinated and those who cannot produce vaccination card or records during the community survey should be vaccinated with rubella-containing vaccine according to the national policy.

3.5.14 Data management

Data analysis

Analysis the CRS surveillance data on a monthly basis, or more frequently if necessary. Epidemiologic variables that should be assessed include the following:

- number of cases reported throughout time frame assessed (e.g. year)
- case classification status
- geographic location of CRS cases within the country
- whether or not cases were clustered and/or associated with rubella outbreaks
- maternal characteristics (age, race/ethnicity, country of birth and vaccination status)
- location of maternal exposure to rubella.

Monitoring indicators

- Surveillance quality assessments need to be conducted at the sentinel sites at least every 6 months to assess completeness of CRS surveillance at the site.
- This should be done by reviewing hospital records by the HSO to identify any missed cases.
- Missed cases can be identified by comparing the list of reported CRS cases with the list of all cases that meet the entry criteria for CRS surveillance (i.e. criteria for suspected CRS cases). The proportion of missed cases at a sentinel site can be assessed as the percent of missed cases identified by the HSO among all cases that meet the CRS surveillance entry criteria (total of both reported and unreported cases).
- Similarly, the proportion of suspected CRS cases that have been reported but have not been tested by the laboratory can be assessed as the percentage of reported cases without laboratory testing among all reported suspected CRS cases (both tested and untested).
- Monitoring surveillance data quality. CRS surveillance case reports should be assessed for any missing variables. If records are incomplete, the findings should be discussed with providers at the site and the need for completeness of data and case reporting should be emphasized.

CRS Indicators

Surveillance attribute	Indicator	Target
Reporting rate	National annual rate of suspected CRS cases $\frac{\text{number of suspected CRS cases for the year}}{\text{live birth cohort of the population in which the cases occurred}} \times 10{,}000$	≥1 per 10, 000 live births
Adequate investigation	Percentage of suspected CRS cases with the following data points completed: name and/or identifier; place of residence, sex, date of birth, date of reporting, date of investigation, date of specimen collection, history of rash illness of mother, travel history of mother, vaccination history of mother, age of mother, clinical examinations for hearing impairment, cataract, and congenital cardiac/heart defects and clinical outcome of the CRS case (alive or dead) $\frac{\textit{number of suspected CRS cases for which an adequate investigation * was initiated after three 3 months of age of the child}}{\text{total number of suspected CRS cases the cases occurred}} \times 100$ * Adequate investigation defined as the collection of the following data points: name and/or identifier; place of residence; sex; date of birth; date of reporting; date of investigation; date of specimen collection; history of rash illness of mother; travel history of mother; vaccination history of mother; age of mother; clinical examinations for hearing impairment, cataract, and congenital cardiac/heart defects and clinical outcome of the CRS case (alive or dead).	≥80%
Laboratory confirmation (adequate specimen rate)	Percentage of suspected cases with adequate blood specimen tested for laboratory confirmation (IgM/ IgG, PCR) in an accredited laboratory $\frac{\textit{number of suspected cases from whom adequate specimens ** for detecting CRS (IgM/IgG) were collected and tested}}{\text{total number of suspected CRS case}} \times 100$	≥80%
	** Adequate specimens for serology are those collected within 12 months of age of the child that consist of ≥ 0.5 ml serum	
Viral detection (adequate specimens for virus detection)	Percentage of confirmed cases with adequate specimens tested for virus detection/isolation $\frac{\textit{number of lab – confirmed CRS cases for the year for whom adequate specimen was analyzed for viral detection}}{\text{total number of suspected CRS case}} \times 100$	≥80%
Monitoring of virus excretion	Percentage of confirmed cases with at least 2 negative tests for virus detection/isolation after 3 months of age with at least a 1month interval between specimen collection	≥80%

	$\frac{\text{number of lab – confirmed CRS cases with at least two negative tests for virus detection after 3 months of age, with at least a 1 – month interval between tests for the year}}{\text{total number of suspected CRS case}} \times 100$	
Timeliness of detection	Percentage of confirmed CRS cases detected within 3 months of birth $\frac{\text{number of confirmed CRS cases (clinical compatible and laboratory confirmed) detected within 3 months of birth}}{\text{total number of suspected CRS case}} \times 100$	≥80%
Timeliness of specimen transport	Percentage of confirmed CRS cases detected within 3 months of birth $\frac{\text{total number of specimens (serologic or virology) received at the laboratory within 5 days of collection}}{\text{total number of specimens (serologic or virology) received for testing in the given year.}} \times 100$	≥80%
Timeliness of reporting laboratory results-Serology	Proportion of serologic results reported by the laboratory within 4 days of receiving the specimen $\frac{\text{total number of serologic results reported by the laboratory within 4 days of receiving the specimen}}{\text{total number of serology specimen received for testing in the given year}} \times 100$	≥80%
Timeliness of reporting laboratory results-Virology	Proportion of virus detection and genotyping results (where appropriate) that are completed within 2 months of receipt of specimen $\frac{\text{total number of virus detection and genotyping results (where appropriate) that are completed within 2 months of receipt of specimen}}{\text{total number of virology specimen received for testing in the given year}} \times 100$	≥80%

3.5.15 Feedback

Provide feedback to stakeholders involved in the CRS surveillance system. Feedback should include information on the status of the epidemiology of CRS including, if necessary, any updates and recommendations for improvements.

3.5.16 Special approach to identify CRS cases

Rubella in pregnancy registries: Rubella in the pregnancy registry can be used for follow-up of pregnant women exposed to rubella and their pregnancy outcome(s) as well as for identification of CRS cases. Rubella in pregnancy registries should be maintained at the local level so that comprehensive follow-up of pregnant women can occur and infants born with CRS can be identified and diagnosed immediately and receive early interventions for any associated defects. The registry should include maternal contact, demographic data and pregnancy outcome (e.g. miscarriage, termination, infant with CRS, etc.).

Linkage to other surveillance: CRS surveillance with laboratory confirmation can be incorporated into country birth defect surveillance if present as part of an enhanced birth defect surveillance system, or into other surveillance systems capturing congenital cataracts/abnormalities.

Retrospective review of medical records: Retrospective medical record review could be used to monitor the sensitivity of CRS surveillance systems annually. Limitation of this approach is that retrospectively identified cases usually lack laboratory confirmation, and therefore lack a definitive diagnosis.

Serological surveys of reproductive age women: Serological assessments of rubella IgG antibody levels among reproductive-age women in a survey setting may help evaluate population immunity against rubella and protection against CRS in newborns. Rubella IgG can be acquired through both vaccination and natural infection, therefore serosurveys are not purely a reflection of vaccination coverage. A serological survey is not a substitute for conducting CRS surveillance, but can provide complimentary information.

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4 Neonatal Tetanus

4.1 Introduction

Tetanus is an acute, often fatal, disease caused by an exotoxin produced by the bacterium *Clostridium tetani*. Clostridium tetani. C. tetani spores (the dormant form of the organism) are found in soil and in animal and human feces. Carle and Rattone in 1884 who first produced tetanus in animals by injecting them with pus from a fatal human tetanus case. During the same year, Nicolaier produced tetanus in animals by injecting them with samples of soil. In 1889, Kitasato isolated the organism from a human victim, showed that it produced disease when injected into animals, and reported that the toxin could be neutralized by specific antibodies. In 1897, Nocard demonstrated the protective effect of passively transferred antitoxin, and passive immunization in humans was used for treatment and prophylaxis during World War I. A method for inactivating tetanus toxin with formaldehyde was developed by Ramon in the early 1920's which led to the development of tetanus toxoid by Descombey in 1924. It was first widely used during World War II[1]. Neonatal tetanus (NT) is a form of generalized tetanus that occurs in newborn. Neonatal tetanus occurs in infants born without protective passive immunity if the mother is not immune. It usually occurs through the unhealed umbilical cord or stump, particularly when the stump is cut with an unsterile instrument. Poor hygiene, social stigma and insufficient preventive health services provide ideal conditions for the causative agent, Clostridium tetani.

Tetanus

Etiology discovered in 1884 by Carle and Rattone

Passive immunization used for treatment and prophylaxis during World War I

Tetanus toxoid first widely used during World War II

4.2 Causative agent

Clostridium tetani is a gram-positive, anaerobic bacterium which forms a spore. The organism is sensitive to heat and cannot survive in the presence of oxygen. The spores, in contrast, are very resistant to heat and the usual antiseptics. They can survive autoclaving at 249.8°F (121°C) for 10–15 minutes.

The spores are also relatively resistant to phenol and other chemical agents[1]. Clostridium tetani produces two exotoxins, tetanolysin and tetanospasmin.

4.3 Pathogenesis

C. tetani usually enters the body through a wound and in neonate through unhealed umbilical stump, particularly when the stump is cut with an unsterile instrument. In the presence of anaerobic conditions, the spores germinate and produce toxin. Toxins disseminate via blood and lymphatics, act at several sites within the central nervous system. The tetanus toxin interferes with release of neurotransmitters, blocking inhibitor impulses and cause typical clinical manifestations.

Clostridium tetani

Anaerobic gram-positive, spore-forming bacteria

Spores found in soil, animal feces

Two exotoxins produced with growth of bacteria

Tetanospasmin estimated human lethal dose = 2.5 ng/kg

This leads to unrestricted muscle contraction and spasm. Seizures may occur, and autonomic nervous system may also be affected.

4.4 Reservoir

Tetanus spores are widely distributed in soil and in the intestine and feces of horses, sheep, cattle, dogs, cats, rats, guinea pigs and chickens. In agricultural areas, human adults may harbor the organism.

4.5 Communicability

Unlike other EPI diseases, infection occurs from exposure to contaminated material rather than from person-to-person spread. Neonatal tetanus may be considered an environmental hazard rather than a communicable disease.

4.6 Transmission

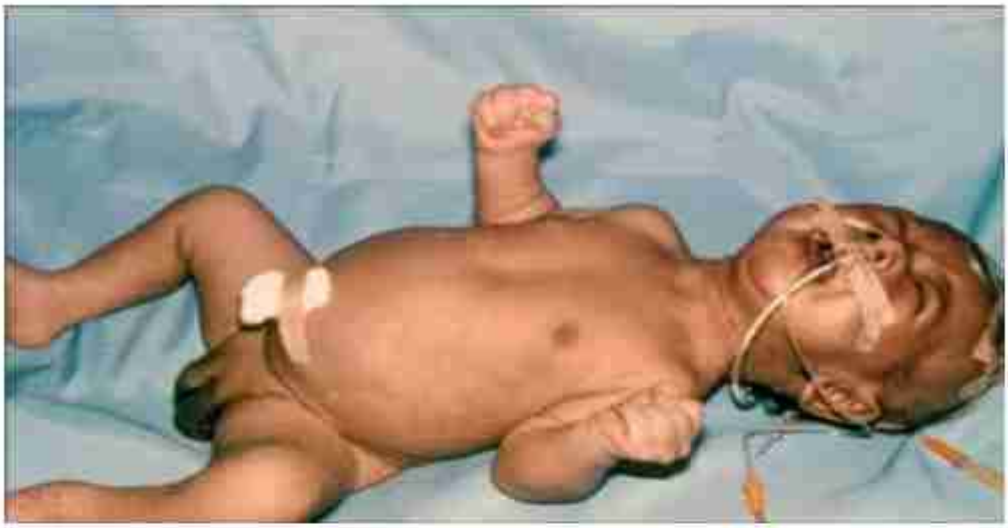
The spores of C. tetani enter the body through direct contact in the wound. In a newborn baby, the portal of entry is via the umbilical cord or stump. Unclean methods of cutting, tying or dressing the cord may allow tetanus spores to enter the baby's bloodstream. Even babies delivered under clean conditions in health facilities may become infected with tetanus spores and die if the mother does not properly care for the umbilical stump at home. Most cases of NT occur between 3 and 14 days of life (day 1 = day of birth).

4.7 Clinical feature of Neonatal Tetanus

The toxins produced by C. tetani may cause sustained focal or generalized involuntary muscle contractions. In neonates, tetanus almost always presents in the generalized form. Usually, the first sign is inability to suck because of spasm of the jaw muscles, which rarely occurs earlier than 3 days of age.

The baby may then cry continuously. The jaw becomes clenched (trismus), causing the baby to have the appearance of a smile (risus sardonicus). Soon afterwards, the baby develops stiffness of the neck and then the entire body, with contraction of the spinal muscles causing the baby to arch its back (opisthotonos). Increasingly violent spasms frequently occur, and convulsive fits can result from the slightest stimulus (sound, light, or touch). The baby's breathing becomes difficult and spasms and convulsive fits become more frequent, usually resulting in death.

Clinical feature
Inability to suck
Baby cries continuously
Jaw becomes clenched (trismus)
Stiffness of neck and then entire body
Contraction of spinal muscle causing baby to arch its back (opisthotonos)
Frequent violent spasms
Convulsive fits with sound and light



4.8 Differential Diagnosis of Neonatal Tetanus

The differential diagnosis of neonatal tetanus includes bacterial meningitis, encephalitis, other causes of neonatal sepsis, muscle spasms due to hypocalcemia, congenital abnormalities, birth injuries.

4.9 Laboratory Diagnosis

No laboratory findings are characteristic of tetanus. The diagnosis is entirely clinical and does not depend upon bacteriologic confirmation. C. tetani is recovered from the wound in only 30% of cases and can be isolated from patients who do not have tetanus.

4.10 Treatment

The principles of treatment of all cases of tetanus are to remove the source of tetanospasmin, to neutralize circulating toxin and to provide intensive supportive care until tetanospasmin has been metabolized by the body. Antibiotics may also be given.

Tetanus Immune Globulin should be administered as quickly as possible. TIG can only help remove unbound tetanus toxin. It cannot affect toxin bound to nerve endings. Supportive care of the neonate ideally includes endotracheal intubation, use of neuromuscular blocking agents and assisted ventilation. When facilities are not available, sedatives and muscle relaxants such as chlorpromazine (3 mg every 6 hours), elixir of phenobarbital (10-20 mg every 6 hours), or elixir of mephenesin (130- 160 mg every 6 hours) may be given orally. Diazepam may be used to control convulsive fits.

4.11 Prevention

Neonatal tetanus can be prevented by ensuring clean conditions during childbirth and clean care of the umbilical stump after birth and by immunizing mothers with Tetanus Toxoid Containing Vaccine (TTCV) before or during pregnancy. Most developed countries have been able to reduce NT incidence to near zero simply by ensuring hygienic child birth and cord care. Clean delivery practices have the added advantage of preventing other puerperal infections as well. It is important to remember, however, that if the baby is born without protective antibody from its

mother, he or she will remain susceptible to tetanus until receiving 2 TTCV (e.g. Penta, DPT, Td) doses.

Immunization of mothers against tetanus remains the more reliable method to prevent NT. Maternal antibodies against tetanus are passively transferred to the fetus via the placenta, thereby conferring immunity against tetanus in the neonate. One dose of tetanus toxoid ensures little, if any protection. Generally, protection begins 2 weeks after the second dose. To get optimum results second dose should be given 4 weeks after the first dose. Table 9 summarizes the recommended schedule for TTCV and the duration of protection for each dose. Tetanus toxin is very potent and requires small amount to cause the disease. However, this amount is insufficient to stimulate antibody production and does not result immunity against tetanus.

Table 10: Tetanus Toxoid Containing Vaccine (TTCV) schedule

Dose	Time of administration	Duration of protection
TTCV 1	At 15 years of age	None
TTCV 2	4 weeks after TTCV 1	3 years
TTCV 3	6 months after TTCV 2	5 years
TTCV 4	1 year after TTCV 3	10 years
TTCV 5	1 year after TTCV 4	Throughout child-bearing years

4.12 NT Surveillance

Neonatal tetanus is primarily a problem of developing countries, where clean obstetric services are not available or not utilized by many women. According to World Health Organization Report in, 2022, the total number of reported Neonatal Tetanus globally was 2076. WHO estimates that in 2015 (the latest year for which estimates are available), 34,019 newborns died from NT, a 85% reduction from 2000.

Table 11: Neonatal Tetanus Global & Bangladesh Annual Incidence, 1980-2022

Area	1980	1990	2000	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Bangladesh	1068	740	376	108	0	117	110	95	84	49	41	33	21
Global	13005	25293	17935	4149	2238	3580	1997	2266	1803	2173	2300	4140	2076

Source for NT: https://immunizationdata.who.int/pages/incidence/TTETANUS.html?CODE=Global+BGD&DISEASE=NTETANUS&YEAR=

In Bangladesh, passive hospital-based surveillance identified only 21 cases of neonatal tetanus in 2022.

4.13 NT Elimination

At the end of the 1980s, neonatal tetanus was considered a major public health problem. WHO estimated that 787,000 newborn children died of neonatal tetanus in 1988, a rate of 6.5 cases per 1000 live births. In 1989, the 42nd World Health Assembly called for elimination of neonatal tetanus by 1995. In 1990, the World Summit for Children listed neonatal tetanus elimination as one of its goals, which was endorsed by the 44th World Health Assembly in 1991. **Elimination is defined as <1 NT case per 1,000 live births at district level per year.**

In Bangladesh, the number of neonatal tetanus deaths has decreased substantially in the past 2 decades. According to national disease incidence surveys conducted in 1986, 1994 and 2000, NT mortality rate per 1,000 live birth was 41, 6 and 2.3 respectively.

Figure 24: Number of NT cases and Incidence- Bangladesh, 2008-2022

With the reduction of reported NT cases a comprehensive review of district level indicators for the risk of NT was conducted in January 2008. Overall, the data supported the claim of elimination, but it was decided that a survey should be done for confirmation. In May 2008, the Ministry of Health and Family Welfare, carried out an evaluation using standard WHO protocol to determine whether neonatal tetanus had been eliminated in Bangladesh. Two community-based surveys were performed in the 2 districts where children were considered to be at the highest risk from neonatal tetanus. According to the survey results Bangladesh has achieved MNT elimination and maintaining the status.

4.14 Strategies for NT Elimination

- Provision of TTCV 5-dose to all child bearing aged women (CBAW)
- Provision of clean delivery services to all pregnant women
- SIA in high risk areas
- Effective surveillance for MNT

4.15 Rationale for surveillance

Every NT case is an event that marks the failure of multiple levels of the health system. The key objective of NT surveillance is to detect cases of NT towards monitoring achievement and

maintenance of elimination. NT surveillance data (or a lack thereof) are used to identify areas and subpopulations at high-risk for NT and guide effective public health response for maternal and neonatal tetanus elimination (MNTE).

4.16 Case Definitions and Final Classifications

Suspected case

A suspected case for NT is a case that meets either of these two criteria:

Any neonate who could suck and cry normally during the first two days of life and developed tetanus-like illness or death between 3 and 28 days of age

OR

Any neonate who died of an unknown cause during the first month of life.

Confirmed case

A confirmed case is any suspected NT case found during case investigation to have all three of the following:

Normal ability to suck and cry during the first two days of life

AND

could not suck normally between 3 and 28 days of age

AND

developed muscle stiffness and/or spasms (jerking).

The basis for case classification is entirely clinical and does not depend on laboratory confirmation. NT cases reported by physicians are considered to be confirmed.

Discarded case

A discarded case is one that has been investigated and does not satisfy the clinical criteria for confirmation or has an alternate diagnosis.

Not investigated

Any suspected case not investigated, or without information available on age and symptoms to confirm the case, should receive the final classification of not investigated.

4.17 Neonatal Tetanus case notification

All Neonatal tetanus cases should be immediately notified to DSFP. All health facilities, private practitioners and other health care providers must immediately report any case of NT (either living or dead) to the respective DSFP. The mother of the NT case should be vaccinated with TTCV as soon as possible once the diagnosis is made regardless of her prior immunization status. The DSFP will send the LSO to investigate the case and take appropriate actions. If the mother lives in a different upazila, municipality, or City Corporation then the local DSFP will notify the concern DSFP to conduct additional case finding activity and case response immunization. SIMO will provide technical assistance, if necessary.

4.18 Types of surveillance

Active surveillance

Major health facilities should be visited regularly (weekly) to identify any NT case admitted or diagnosed there. Such visits should preferably be made by Local Surveillance Officer along with Surveillance & Immunization Medical Officer. During these visits, hospital in-patient and out-patient registers should be checked and key clinical staff (e.g. in paediatric, emergency unit/s and isolation ward/s) should be asked whether any new NT case has been identified in the hospital since previous visit.

Passive Surveillance

Designated reporting sites at all level should report all cases of NT along with other reportable VPDs even if there are no cases ("zero reporting") through AFP and VPD weekly form for hospitals.

Community Surveillance

All field workers under Ministry of health and family welfare and NGO should immediately bring the suspected NT case to the upazila health complex or NGO clinic for treatment and to report.

All neonatal death should be reported to immediate supervisor (HI, AHI or FPI or NGO supervisor) in the field and should be investigated by Medical Officer to identify NT.

Any neonatal death between 3-28 days of age in which the cause of death is unknown will be considered as a suspected NT Case.

4.19 NT case investigation and response

Investigation and response to NT case confirmed at facilities or reported by field workers should follow a stepwise approach:

Step 1: Interview the mother, examine the infant (if living) and complete the "Neonatal Tetanus Case Investigation Form" *(Annexure 13)*.

Step 2: Vaccinate the mother with TTCV regardless of previous vaccination status if vaccination has not already done following identification of NT. Last does received prior to development of NT of her child to be considered as invalid or did not work. Therefore, this dose to be repeated and complete the series, if eligible for, as per national EPI schedule.

Step 3: Mobilize members of the investigation and response team to the village or neighborhood of the NT case with additional NT Case Investigation Forms, women Registration Book (for TTCV), adequate supply of vaccine and logistic (TTCV vials, AD syringes, safety boxes and women card etc.).

Step 4: Ask village doctors, pharmacists, homeopaths, NGO workers local leaders etc. if additional cases of NT or neonatal deaths (NDs) occurred in 3-28 days old babies in the past 6 months.

Step 5: Investigate any additional cases of NT or ND and vaccinate the mothers of NT cases.

Step 6: Conduct house-to-house visits in the entire sub block/ urban mahalla of the index case home to identify women of childbearing age who are eligible to receive TTCV. Record the findings on the worksheet on the back of the Neonatal Tetanus Case Investigation Form *(Annexure 09)*. **All eligible CBA women *(as per national 5 doses schedule)* to receive TTCV in the rural sub-block or urban mahalla of the index NT case within a week of reporting**. Advice unvaccinated women to attend the next scheduled EPI outreach session; be sure to tell any woman receiving her 1st dose of TTCV must receive a 2nd dose a month later to be protected against tetanus.

Step 7: All eligible CBA women of **remaining 7 rural sub blocks of ward or remaining mahalla of Urban ward of the index NT case to be vaccinated with TTCV within a month of case reporting.** Vaccinate all eligible CBA women of that area and register the doses in the TTCV Registration Book; advice unvaccinated women to attend the next scheduled EPI outreach session; be sure to tell any woman receiving her 1st dose of TTCV must receive a 2nd dose in one month to be protected against tetanus.

Step 8: Anticipate increased TTCV vaccine needs for the next scheduled EPI vaccination session.

After case investigation and response activities the case investigation form along with the case response immunization information should be sent to EPI headquarter.

4.20 Contact tracing

As tetanus is not contagious, no contract tracing is needed

4.21 Surveillance performance indicators

1. Surveillance Attribute: Completeness of reporting

Indicator: Percentage of facilities reporting NT data even zero reporting

Target: ≥90%

Calculation:

$$\frac{\text{Number of facilities reporting NT}}{\text{Total number facilities}} \times 100$$

2. Surveillance Attribute: Timeliness of reporting

Indicator: Percentage of facilities reporting NT data on time, even in the absence of cases (zero reporting)

Target: ≥80%

Calculation:

$$\frac{\text{Number of facilities reporting by the deadline}}{\text{Total number facilities}} \times 100$$

3. Surveillance Attribute: Completeness of case investigation

Indicator: Proportion of suspected NT cases investigated

Target: ≥90%

Calculation:

$$\frac{\text{Number of Suspected NT case investigated}}{\text{Total number of reported suspected NT cases}} \times 100$$

4. **Surveillance Attribute:** Timeliness of case investigation

Indicator: Proportion of cases investigated within 48 hours of notification

Target: ≥80%

Calculation:

$$\frac{\text{Number of suspected NT cases investigated within 7 days of notification}}{\text{Total number of suspected AFP case}} \times 100$$

5. **Surveillance Attribute:** Adequate case response

Indicator: Proportion of confirmed NT cases for which adequate response (e.g. CRI) conducted within 7 days of notification

Target: ≥100%

Calculation:

$$\frac{\text{\# NT cases in which mothers received TTCV dose in conjunction with case detection or investigation}}{\text{total \# of NT case investigations}} \times 100$$

6. **Surveillance Attribute:** Achievement and Maintenance of MNTE

Indicator: Percentage of districts with <1 NT case per 1,000 live births

Target: ≥100%

Calculation:

$$\frac{\text{\# Districts with < 1 NT case per 1 000 live births}}{\text{Total number of Districts}} \times 100$$

References:

1. *Epidemiology and Prevention of Vaccine- preventable diseases, CDC, USA*
2. *https://www.who.int/immunization/diseases/MNTE_initiative/en/*
3. *https://www.who.int/immunization/monitoring_surveillance/data/gs_gloprofile.pdf?ua=1*
4. *WHO Vaccine-Preventable Diseases Surveillance Standards-Neonatal Tetanus*
5. *https://www.cdc.gov/vaccines/pubs/pinkbook/tetanus.html*

5. Tetanus after neonatal period

5.1 Introduction

Tetanus is an acute, often fatal disease caused by an exotoxin produced by Clostridium tetani. Tetanus is a non-communicable preventable disease, not transmitted from one person to another.

In Bangladesh total 257 cases of tetanus were after the neonatal period was reported in 2017 through Passive Surveillance. Over the period there is gradual decline in number of tetanus cases and last case was reported in 2020.

Table 12: Tetanus cases after neonatal period Global & Bangladesh, 1980-2022

Year	1980	1990	2000	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Global	100931	39444	5776	9383	10293	6758	11816	10243	13300	12572	9597	5661	4575
Ban	1787	1771	779	400	0	442	331	257	142	117	19	0	0

Source: https://immunizationdata.who.int/pages/incidence/TTETANUS.html?CODE=Global+BGD&DISEASE=TTETANUS+NTETANUS&YEAR=

5.2 Epidemiology of Tetanus

Details regarding the causative agent and its reservoir and communicability have been described in NT chapter.

Epidemiology

- Reservoir: Soil and intestine of animals and humans
- Transmission: Contaminated wounds, Tissue Injury
- Temporal pattern: Peak in summer or wet season
- Communicability: Not contagious

5.3 Prevention

Prevention of tetanus after the neonatal period also requires vaccination of the infant, children or adult with Tetanus Toxoid containing vaccine (TTCV). For infants, Tetanus Toxoid is administered together with pertussis, diphtheria, Hepatitis-B and Haemophilus influenzae type B (Hib) vaccine in the form of Penta-valent. Infants should receive 3 doses of Penta-valent with the first dose at or after 6 weeks of age; the 2nd dose should be given 28 days after the 1st dose and the 3rd dose 28 days after the 2nd dose. Three doses of Penta-valent should protect the child against tetanus for 3 years.

All women should get 5 doses of TT/Td according to the TT/Td-5 doses schedule starting from the age of 15 to protect them as well as their future newborn children from tetanus. A woman who has completed a total of 5 doses of TT/Td according to the TT/Td-5 dose schedule is considered to be protected throughout her child-bearing age and does not require to repeat vaccination during this time period.

Persons beyond EPI target include adult men and all persons 50 years of age and older should receive TT/Td every 10 years to remain protected against tetanus.

Tetanus Toxoid

- Formalin-inactivated tetanus toxin
- Schedule
  - three or four doses plus booster
  - booster every 10 years
- Efficacy
  - approximately 100%
- Duration
  - approximately 10 years
- Should be administered

Tetanus prophylaxis in patients with wounds is based on careful assessment whether the wound is clean or contaminated and the immunization status of the patient. In general, a patient with an unknown vaccination history or with less than 3 doses of TT/Td in the past should always receive TT/Td prophylaxis after any injury. Tetanus Immune Globulin (TIG) is indicated only for persons with an unknown vaccination history or <3 TT/Td doses and who have deep or dirty wounds. If a patient has certain evidence of 3 or more doses of TT/Td, then TT/Td is needed only if it has been more than 10 years since the last TT/Td dose for clean minor wounds or more than 5 years for serious or dirty wounds. In addition, wound cleaning and, if indicated, surgical debridement and antibiotics are also important components of wound management.

Table 13: Tetanus Prophylaxis in Routine Wound Management

Previous Tetanus Immunization (doses)	Clean minor wounds		All other wounds	
	Give TT/Td[1]	Give TIG	Give TT/Td[1]	Give TIG
Unknown or less than 3	Yes	No	Yes	Yes
3 or more	No[§]	No	No[‡]	No

[1]For children younger than 7 years, give tetanus toxoid as Penta; for > 7 years of age, Td is preferred to TT alone as it also provides booster protection against diphtheria.

[§]Yes, if more than 10 years since last dose

[‡]Yes, if more than 5 years since last dose

5.4 Clinical Aspects of Tetanus after the Neonatal Period

Tetanus is characterized by painful muscular contractions. The disease usually presents with a descending pattern. The first sign is trismus or lockjaw, followed by stiffness of the neck, difficulty in swallowing and rigidity of abdominal muscles. Other symptoms include elevated temperature, sweating, raised blood pressure and episodic rapid heart rate.

Generalized spasms occur, frequently induced by sensory stimuli and last for several minutes; typical features of tetanic spasms are opisthotonus and a facial expression known as "risus sardonicus".

Cephalic tetanus is a rare form of the disease, occasionally occurring with otitis media (ear infections) in which C. tetani is present in the flora of the middle

Clinical Feature

- Spasms and stiffness in your jaw muscles (trismus)
- Stiffness of your neck muscles
- Difficulty swallowing
- Stiffness of your abdominal muscles
- Painful body spasms lasting for several minutes, typically triggered by minor occurrences, such as a draft, loud noise, physical touch or light

ear or following injuries to the head. There is involvement of the cranial nerves, especially in the facial area.

5.5 Complications

Laryngospasm (spasm of the vocal cords) and/or spasm of the muscles of respiration lead to interference with breathing. Fractures of the spine or long bones may result from sustained contractions and convulsions. Aspiration pneumonia is a common late complication of tetanus cases.

5.6 Laboratory Diagnosis

The diagnosis is entirely clinical and does not depend upon bacteriologic confirmation or any other laboratory findings.

5.7 Treatment

Treatment of patients with tetanus consists mainly of supportive care until the toxin is metabolized and degraded in the body. Supportive care includes placing the patient in a dark, peaceful location without external stimuli, control of involuntary spasms without limiting voluntary movement, nutritional support and, if needed, respiratory support. Benzodiazepines are the drug of choice to keep the patient calm and reduce muscle contraction. In severe cases neuromuscular blockade along with assisted ventilation and tracheostomy may be required. In addition to supportive care, human TIG (3,000-6,000 units) may be given IM in a single dose to prevent any additional toxin reaching the CNS. Elimination of the organism (Clostridium tetani) and the possibility of further toxin production may be done with antibiotic therapy (penicillin and metronidazole) and surgical drainage or debridement when necessary.

5.8 Case-fatality

The case-fatality rate ranges from 10% to 90%, it is highest in infants and elderly, and varies inversely with the length of incubation period and the availability of experienced intensive care unit personnel and resources.

5.9 Post-Neonatal Tetanus Surveillance

5.9.1 Definition of Tetanus (after Neonatal Period)

Acute onset of hypertonia and/or painful muscular contractions of the jaw or neck and Generalized muscle spasms, and

Without other apparent medical causes determined by a physician.

5.9.2 Tetanus Case Notification

Unlike neonatal tetanus, cases of tetanus occurring after the neonatal period do not need to be reported immediately to public health authorities, but they still should be reported.

Better understanding of tetanus epidemiology is necessary to determine geographic and demographic risk factors for tetanus deaths in Bangladesh and to develop immunization strategies for more effective prevention of tetanus morbidity and mortality.

Reporting of all Tetanus (after neonatal period) cases should be done by attending doctors of the hospital/clinic through AFP and EPI disease report form. The filled report form to be submitted to Hospital Surveillance Officer (HSO) in the same day. HSO should include the data of the case in the weekly line listing and send to the DSFP.

As tetanus is not a communicable disease, no protective measures for close contacts are needed.

References:

1. *National AFP and Vaccine Preventable Diseases Surveillance Guideline, 3rd edition, Bangladesh*
2. https://www.cdc.gov/vaccines/pubs/pinkbook/tetanus.html

6. Japanese Encephalitis

6.1 Introduction

Japanese encephalitis (JE) virus is the leading cause of vaccine-preventable encephalitis in Asia and the western Pacific. The first case of Japanese encephalitis viral disease (JE) was documented in 1871 in Japan. Most people infected with JE do not have symptoms or have only mild symptoms. However, a small percentage of infected people develop inflammation of the brain (encephalitis), with symptoms including sudden onset of headache, high fever, disorientation, coma, tremors and convulsions. About 1 in 4 cases are fatal.

6.2 Causative agent

JEV is a single-stranded RNA virus, one of 70 viruses in the Flavivirus genus of the family Flaviviridae. JEV is related to West Nile, Murray Valley encephalitis, dengue, Zika, yellow fever and St. Louis encephalitis viruses. JEV is categorized in 5 genotypes. The major JEV genotypes have varying overlap in geographical distribution but all belong to the same serotype and are similar in terms of virulence and host preference. While genotype 3 used to be the predominantly circulating genotype, there has been a shift towards circulation of genotype 1. The envelope glycoprotein of JEV contains the major epitopes recognized by neutralizing antibodies.

JE Virus

RNA virus

Member of Flaviviridae family

related to dengue, yellow fever and West Nile viruses, Saint Louis encephalitis viruses

Five genotypes

6.3 Pathogenesis

In humans, following an infectious mosquito bite, initial viral replication occurs in local and regional lymph nodes. Viral invasion of the central nervous system occurs probably via blood causing infection and subsequent illness.

Reservoir

Pigs and birds serve as reservoirs and amplifying hosts. They are usually unaffected by the infection. Other domesticated animals, such as horses, cattle, dogs, sheep, cows, chicken and peri-domestic rodents may become infected but do not develop levels of viraemia to support viral amplification. Man is an incidental host of the JEV. They are dead end hosts and do not contribute to the transmission cycle.

6.4 Transmission

JEV is transmitted to humans through the bite of an infected mosquito. The virus is transmitted by Culex mosquitoes and circulates in an enzootic cycle in pigs and wading birds which serve as amplifying hosts. Culex tritaeniorhynchus, the most important vector species, breeds in water pools and flooded rice fields and bites mainly at night. The mosquitoes bite infected animal and birds and in turn become infected with JEV. Humans get infected following a bite by an infected mosquito. However, because humans do not get high levels of JEV in their blood, they cannot further infect any mosquitoes; as a result, human-to-mosquito-to-human transmission does not occur.

Transmission

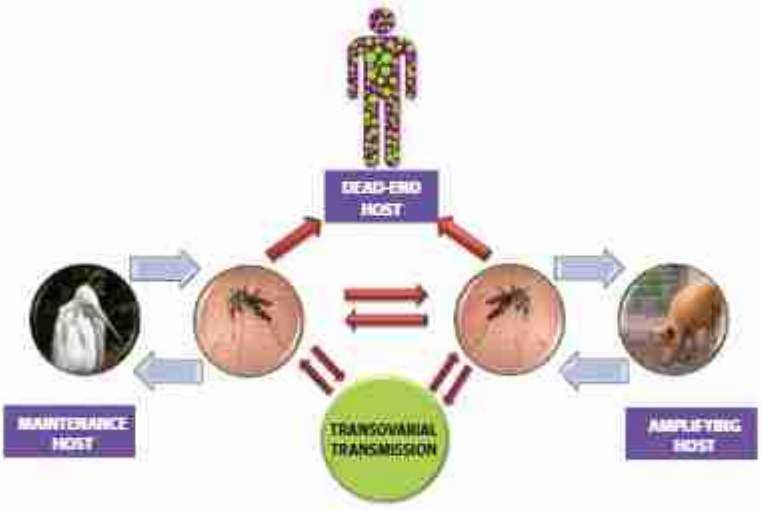
Domestic pigs and wild birds are reservoirs

Virus exists in a transmission cycle between mosquitoes, pigs and/or water birds (enzootic cycle).

Spread by the bite of infected mosquitoes, primarily Culex spp (Culex tritaeniorhynchus).

Human are incidental dead-end hosts. JE virus cannot spread directly from person to person.

Transmission cycle of JE virus



In temperate locations, JEV transmission typically starts in April or May, and lasts until September or October. In tropical and subtropical areas, transmission exhibits less seasonal variation, or intensifies with the rainy season. Where irrigation permits mosquito breeding throughout the year, transmission may occur even in the dry season. The risk of JEV infection is highest during and just after rainy seasons. This is because mosquito populations tend to increase suddenly during the rainy season.

In endemic areas, children 1-15 years old are most frequently infected with JE. In general, JE cases are infrequent among children younger than 1, mainly, it is believed, because they have less exposure to mosquitoes. Adult infection most often occurs in areas where the disease is newly introduced because there is no established immunity among the population.

Population at risk

Primarily affects children

People with weakened immune systems

Seasonality

Usually peaks in summer and fall (April to October)

Seasonal transmission varies with monsoon rains and irrigation practices

JE is typically found in rural areas with abundant rice cultivation. People living in rural areas Seasonal transmission varies with monsoon rains and irrigation practices where rice is grown, and pigs are raised face the highest risk. Being outdoors after sunset is a risk factor since mosquitoes commonly bite in the twilight hours. Cases have been detected in cities, such as Kathmandu and New Delhi, in the absence of rural travel, possibly suggesting expansion of the area of JEV transmission due to changing land use patterns or vector adaptation.

6.5 Clinical features

Most JEV infections are asymptomatic. One case of encephalitis is estimated to occur for every 300 JEV infections. Host factors that result in infection progressing to illness are not known. After an incubation period of 4–14 days clinical symptoms follow, mostly characterized by sudden onset of high fever, chills, headache, myalgia, mental confusion and opisthotonus, and acute flaccid paralysis may occur. The clinical picture of infection has 4 stages; prodromal, acute, subacute, and convalescence. The prodromal stage lasts from 2 to 3 days and has a high fever with severe headache. Non-specific symptoms include malaise, anorexia, nausea and vomiting.

Clinical features

Most human infections are asymptomatic or only mild symptoms.

<1% of people infected with JE virus develop clinical disease

Symptoms (after 1/2 weeks)

sudden onset of headache

high fever

Seizures

disorientation

coma

paralysis

tremors and

convulsions

30%–50% of people with encephalitis develops permanent neurologic or psychiatric sequelae

In the acute phase, lasting 3 to 4 days, the patient develops a change in the state of consciousness, which can range from mild clouding to stupor and coma. It is during this phase that patients frequently present for health care. Seizures are common, and the patient remains febrile with weakness and stiff neck is frequently seen. Less commonly observed are tremor, abnormal movements and cranial nerve involvement. Clinical descriptions from India describe focal neurological deficits as a defining characteristic to differentiate Japanese encephalitis from other etiologies. Fatal cases usually deteriorate rapidly at this stage and die.

Convulsions occur in >75% of paediatric patients, though less frequently in adults. In children, gastrointestinal pain and vomiting may be the dominant initial symptoms. Disease may rapidly progress to severe encephalitis with mental disturbances, general or focal neurological

abnormalities and progressive decline in consciousness to coma. Patients may require ventilator support.

The sub-acute phase lasts 7 to 10 days and in uncomplicated cases the fever decreases over a period of 1-2 weeks and neurological sequelae may improve. In severe cases, secondary infections are common during this phase including bladder infections, pneumonia, and bedsores. Close attention by caregivers can minimize these problems.

During the convalescence phase mild cases may recover completely over the next several weeks. Severe cases may improve somewhat but are frequently left with neurological sequelae. Late developing sequelae have also been described such as optic nerve degeneration and seizures.

Among severe cases, about 30% of the surviving patients have serious residual neurologic, psychosocial, intellectual and/or physical disabilities, with a higher rate of sequelae reported for children. Case-fatality in clinical cases is estimated to be around 20%–30%, with young children (<10 years) having a greater risk of severe disease and a higher case-fatality rate.

The clinical presentation of JE cannot accurately be differentiated from other etiologies of meningoencephalitis and requires laboratory diagnostic confirmation. Interestingly, in Vietnam 55% of patients identified with acute flaccid paralysis (AFP) were actually later diagnosed with JE.

6.6 Disability

Disability and sequelae have been found in 40-75% of surviving JE patients. Sequelae fit into 4 major categories: motor, behavior, intellectual and other neurological. Motor deficits are common in ~30% of survivors with significant cognitive and language impairments in 20%. From a study in Thailand, fine motor disability, aggressiveness, uncontrolled emotion/impulsiveness, and abnormal intelligence were the most common sequelae occurring in greater than 70%.

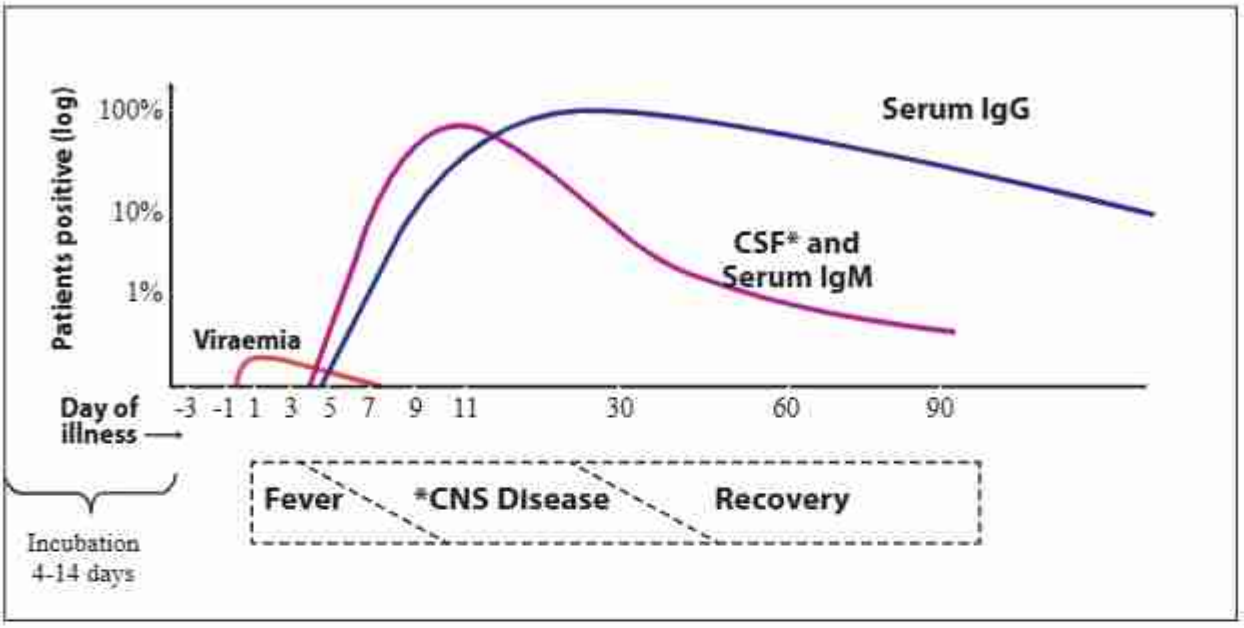
6.7 Diagnosis

Because JE cannot be distinguished clinically from other causes of encephalitis, all cases of acute encephalitis syndrome (AES) or suspected JE should be tested. As the preferred method for laboratory confirmation, WHO recommends testing for JEV-specific IgM antibody in a single sample of cerebrospinal fluid (CSF) or serum, using an IgM-capture ELISA. A serum sample to be obtained at admission. Because an early initial serum sample may have been taken before antibody is produced, if the first sample is negative for JEV-specific IgM, a second serum sample may be collected and tested at discharge, on the 10th day after illness onset, or at the time of death. Antibodies begin to appear soon after onset, but only about 70-75% of patients have IgM antibody in specimens collected up to 4 days after onset. However, all patients will have antibody 7-10 days after onset.

JEV-specific IgM due to JEV infection or JE vaccination may still be detectable in the serum for an unknown period after infection or vaccination (Figure 21). In JE-endemic areas where there are many asymptomatic JEV infections or in areas where vaccination is ongoing, JEV-specific IgM may be present in the serum of AES cases, but encephalitis is not really due to JEV infection. To avoid implicating JEV as the cause, sterile collection and testing of a CSF sample from all persons with AES is recommended when feasible. In such cases, IgM antibody should not be present in the CSF

because there is no viral replication in the brain. When a wild-type JEV causes encephalitis, there is viral invasion of the brain and IgM is produced in the CSF.

Figure 25: JEV-specific IgM due to JEV infection or JE vaccination

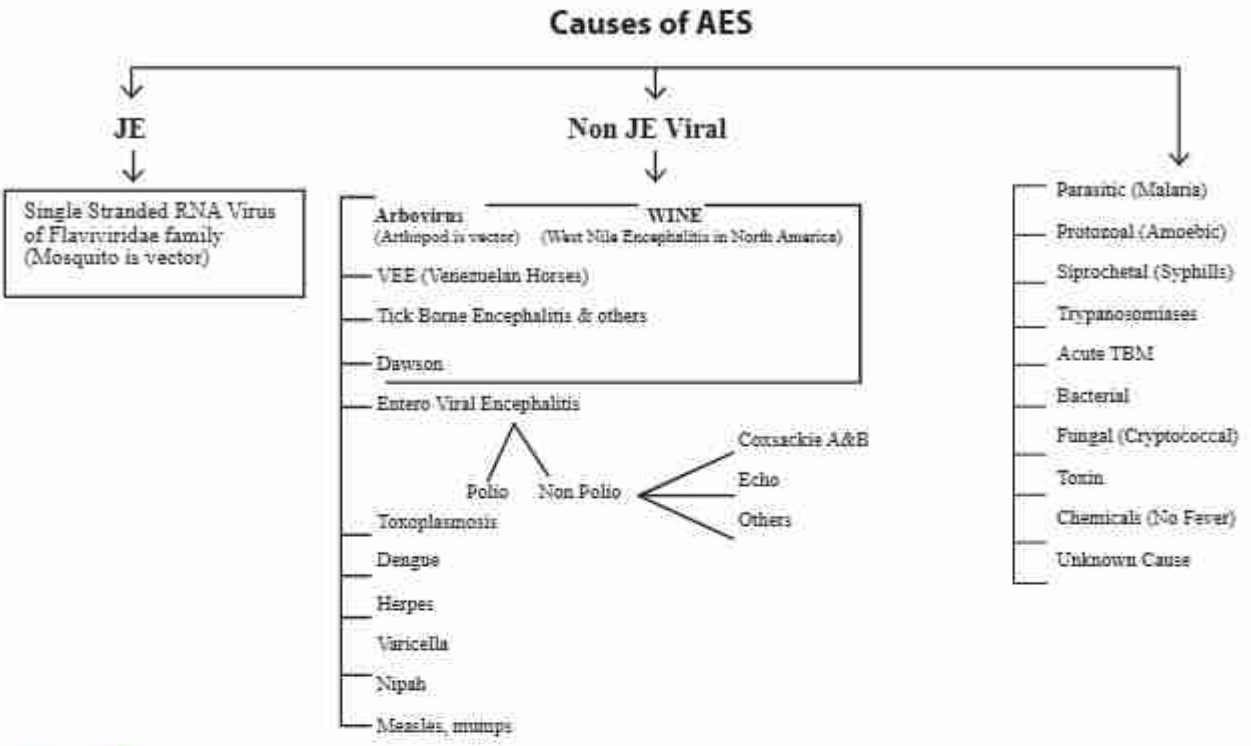


Other methods of diagnosis suitable for use in the field include haemagglutination inhibition (HI) and plaque reduction neutralization assay (PRNT), carried out on paired sera for the demonstration of a significant rise in JEV-specific antibody.

For persons vaccinated with JE vaccine within six months of illness onset, testing a single serum sample for JE IgM may not be diagnostic because it may give a false positive result. In such cases, a diagnosis can only be confirmed by demonstrating JE IgM in the CSF, JE virus isolation, a positive nucleic acid amplification test, immunohistochemistry, or a four-fold or greater rise in antibody titer in acute and convalescent phase serum samples.

Efforts should be made to identify other causes of AES. As a general rule, persons with acute encephalitis should undergo a lumbar puncture to obtain CSF to identify other treatable agents that may result in an illness that manifests as acute encephalitis syndrome. CSF with WBC = 1 000/mm^3 is unlikely to be due to JE or any other arbovirus; in these cases, bacterial causes of purulent meningitis such as Haemophilus influenzae, Neisseria meningitidis, or Streptococcus pneumoniae should be considered. In malaria transmission areas, malaria testing should be carried out to rule out cerebral malaria.

Health care providers should also rule out herpes encephalitis, if possible, as it is a treatable cause of AES.



6.8 Treatment

No specific treatments have been found to benefit patients with JE, but hospitalization for supportive care and close observation is generally required. Treatment is symptomatic. Rest, fluids, and use of pain relievers and medication to reduce fever may relieve some symptoms[2]. It is also important to exclude other causes of CNS affliction, such as meningitis or cerebral malaria, which require specific treatment.

The main causes of JE-related mortality are aspiration, hypoxia, hypoglycemia, uncontrolled seizures, raised intracranial pressure and hypoglycaemia. Supportive care to protect the lungs from aspiration, to maintain breathing with artificial ventilation if necessary, and to prevent or stop seizures are the keys to improved survival once encephalitis has developed. Among patients who develop encephalitis, 20% – 30% die and after recovery from acute illness, 30%-50% of survivors continue to have neurologic, cognitive, or psychiatric symptoms.

6.9 Prevention and Control

Personal Protection Measures

The most effective way to prevent infection from Japanese Encephalitis virus is to prevent mosquito bites. Mosquitoes bite during the day and night. Use of insect repellent, wear long-sleeved shirts and pants, treat clothing and gear, and get vaccinated before traveling, if vaccination is recommended.

Vaccines

Immunization is the best way to prevent Japanese encephalitis. JE vaccines fall into four classes: inactivated mouse brain-derived vaccines, inactivated Vero cell-derived vaccines, live attenuated vaccines and live recombinant (chimeric) vaccines.

The following vaccine dosing schedules and age of administration are recommended. The need for a booster dose in endemic settings has not been clearly established for any of the vaccines listed below.

1. Inactivated Vero cell-derived vaccine: Primary series according to manufacturer's recommendations (these vary by product), generally two doses at 4-week intervals starting the primary series at ≥6 months of age in endemic settings.

2. Live attenuated vaccine: Single dose administered at ≥8 months of age.

3. Live recombinant vaccine: Single dose administered at ≥9 months of age.

4. Preferably, inactivated mouse brain-derived vaccines should be replaced by the newer generation JE vaccines mentioned above.

Control programs for JE focus in three major areas; mosquito control, amplifying host (pig) control, and vaccination. However, neither mosquito control, nor amplifying host (pig) control has been proven to be effective public health measures to control disease.

6.10 Acute Encephalitis Syndrome Surveillance (AES)

Japanese Encephalitis (JE) leading cause of viral encephalitis is a vector-borne viral disease of the brain caused by a mosquito-borne flavivirus. Globally, over 68,000 cases are reported annually with 10,000-15,000 deaths. This figure is believed to represent only a small proportion of the disease burden that actually exists due to incomplete surveillance in many affected areas.

An estimated 3 billion people live in the 24 countries in the WHO South-East Asia and Western Pacific Regions where JE virus (JEV) is transmitted to humans. In these 24 endemic countries, the overall JE incidence for all age groups is 1.8/100,000 but, in children less than 15-years-old, the overall JE incidence is 5.4/100,000. Because of the severity of disease, it is one of Asia's leading causes of long-term neurologic disability. Among patients who develop encephalitis, 20% - 30% die. Among survivors, although some symptoms improve after the acute illness, 30%-50% of survivors will have JE-related disability including intellectual, behavioral, and neurological sequelae. Because of the long-lasting neurologic residua, JE is recognized as a major public health problem in Asia.

Among infected people who develop encephalitis, it begins with the sudden onset of high fever, chills, headache, muscle pain, and confusion. It can progress to cause severe movement disorders or acute flaccid paralysis that can be confused with polio. Convulsions occur in >75% of paediatric patients, though less frequently in adults. There is no specific antiviral treatment for JE. Supportive care to protect the lungs from aspiration, to maintain breathing with artificial ventilation if necessary, and to prevent or stop seizures are the keys to improved survival once encephalitis has developed.

Human vaccination is the only method that has been proven to control of JE. WHO's 5th and 6th SEARO-WPRO Bi-regional, meetings recommended that, as human vaccination is the only effective long-term control measure against JE, all at-risk populations should receive a safe and efficacious vaccine as part of their national immunization program. There is little evidence to support a reduction in JE disease burden from interventions other than vaccination of humans, such as vaccination of pigs, environmental management for vector control, and chemical control of vectors.

6.10.1 Geographic Distribution Disease Burden

Globally human cases of JE have been identified in 24 countries

JE burden distribution map

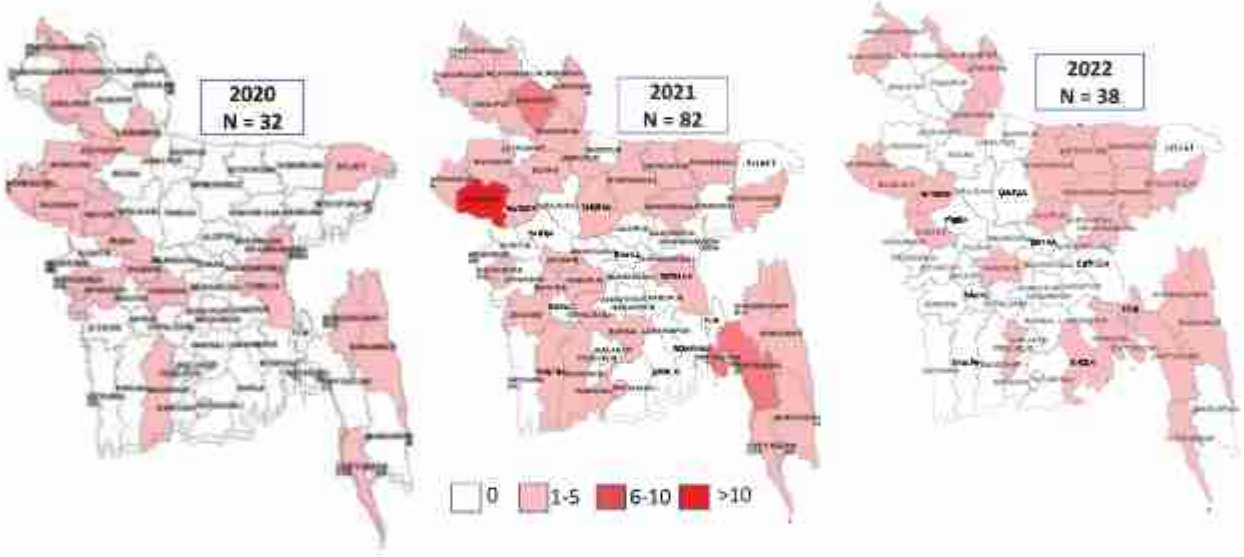
Countries in which Japanese Encephalitis has been identified

Australia	Bangladesh	Bhutan	Brunei Darussalam
Myanmar	Cambodia	China	India
Indonesia	Lao People's Democratic Republic	Japan	Malaysia
Nepal	North Korea	Thailand	Papua New Guinea
Philippines	Russia	Singapore	South Korea
Sri Lanka	Taiwan		

6.10.2 Japanese Encephalitis in Bangladesh

Bangladesh started JE sentinel surveillance in three tertiary care hospitals in 2007 and added a fourth hospital in 2010. The highest numbers of cases are detected in northern districts of the country. These data may not be fully representative of JE burden. JEV transmission resulting in acute encephaliti s syndrome may occur in other districts but not recognized due to complexities and limited availability of serologic testing for JE. In 2017 AES surveillance started involving existing AFP and VPDs surveillance platform. All govt. medical colleges and district hospitals and few major private hospitals were brought under the AES surveillance network to understand disease incidence and disease burden in the country. With this expansion of surveillance network across the country JEV circulation identified in all divisions and most of the districts.

Figure 26: JE Cases by Districts, 2020-2022



6.10.3 Surveillance for Japanese Encephalitis

Goal

To define the disease burden and provide information to guide programmatic interventions.

Objectives

- To characterize the epidemiology
- Detect early warning signals for an impending outbreak
- Strengthen laboratory services for serum and CSF diagnostic assessment
- Assess impact of vaccination as well as to guide future strategies
- To identify high risk geographic areas and populations
- To document the impact of control measures
- To monitor mortality and morbidity

6.10.4 AES Surveillance

Infection with JE virus may be asymptomatic or may cause febrile illness, meningitis, myelitis or encephalitis. Encephalitis is the most commonly recognized presentation and is clinically indistinguishable from other causes of an acute encephalitis syndrome (AES). Syndromic surveillance therefore aims to identify patients with AES and among these confirm JE infection using standard laboratory techniques.

6.10.4.1 Case definition and final classification

Suspected case definition for case finding

Because JE cannot be distinguished from encephalitis due to other causes on clinical grounds alone, a syndromic approach is used in identifying cases. A suspected JE case is a person meeting the definition of AES.

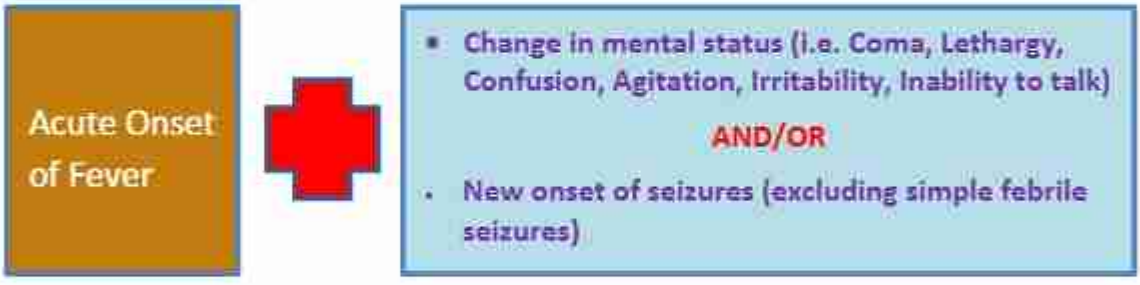
The AES clinical case definition is a person of any age at any time of year with the acute onset of fever and at least one of the following:

A change in mental status (including symptoms such as confusion, disorientation, coma or inability to talk)

OR

New onset of seizures (excluding simple febrile seizures).

A simple febrile seizure is defined as a seizure that occurs in a child aged 6 months to <6 years old, whose only finding is fever and a single generalized convulsion lasting less than 15 minutes, and who recovers consciousness within 60 minutes of the seizure.



AES might have reduced sensitivity for JE among children in some settings. In a study in Vietnam, some children with laboratory-confirmed JE presented with signs of meningitis only (like neck stiffness) or acute limb paralysis only. Overall, the AES case definition captured two-thirds of children with JE; sensitivity among adults was 100%, though the numbers were small. Dengue virus (DENV) infections may be captured in AES surveillance due to the low specificity of the AES case definition, and case presentations can overlap.

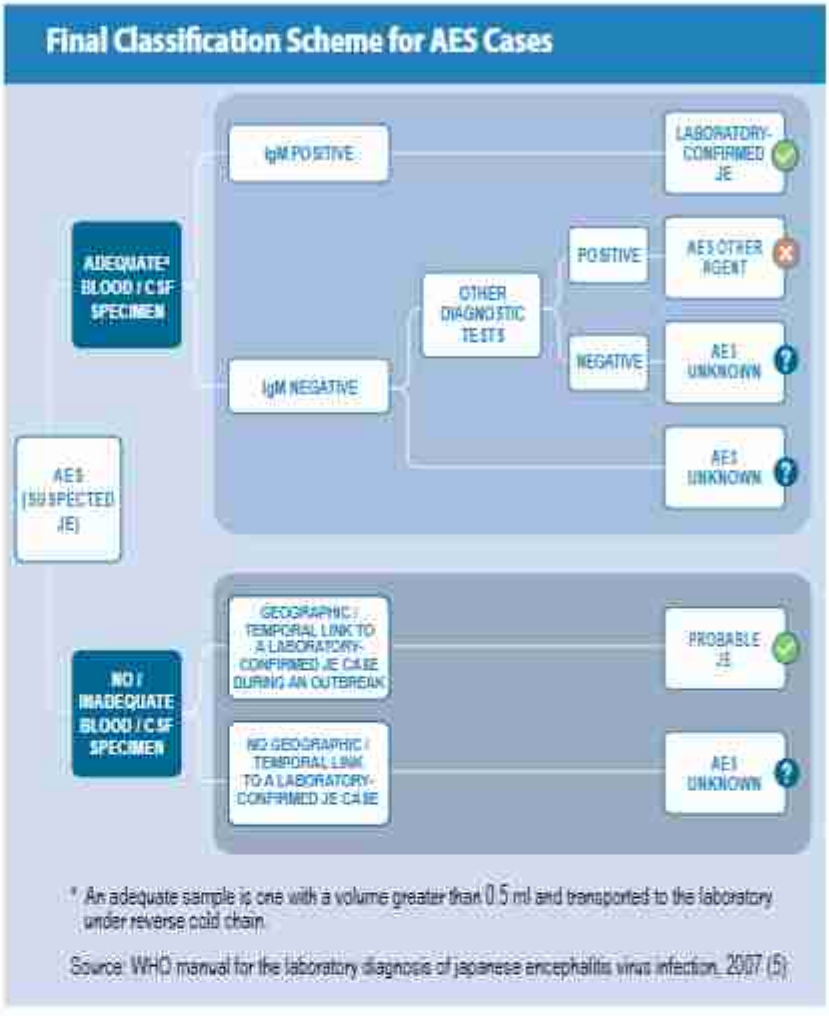
Final case classification

Laboratory-confirmed JE: An AES case that has been laboratory-confirmed as JE.

Probable JE: An AES or suspected JE case that occurs in close geographical and temporal relationship to a laboratory-confirmed case of JE, in the context of an outbreak.

AES – other agent: An AES case in which diagnostic testing is performed and an etiologic agent other than JE virus is identified.

AES – unknown: An AES case in which no diagnostic testing is performed or in which testing was performed but no etiologic agent was identified, or in which the test results were indeterminate.



AES Surveillance

JE surveillance should be conducted throughout the year. While JE transmission shows some seasonality but may occur year-round due to many other pathogens. The surveillance platform may consider detecting other causes of AES besides JE.

6.10.4.2 Active AES Surveillance

Nationwide, case-based AES surveillance with laboratory confirmation is crucial and the best source of information understanding JE disease burden.

One of the most critical units in the reporting system is the health facility. Case-finding through retrospective review of registries and discussion with health care personnel in the emergency, paediatric, medical, neurology and outpatient clinics are critical to the success of active surveillance. The Local Surveillance Officer (LSO i.e. MOCS/MO-DC) along with SIMO responsible to visit the assigned health facility at least once a week to ensure that AES cases are reported that had have occurred in the previous week, encourages reporting from private doctors and looking for new cases. Each visit is to be documented by signing the registers and other relevant documents that are checked. The LSO and/or SIMO will complete the "AFP, NT, Measles, CRS and

AES" Weekly Active Surveillance Form *(Annexure 04)* and submit the report, including "a count of ZERO" to EPI HQ. The report is to reach EPI HQ by Tuesday of next epidemiological week.

6.10.4.3 Passive Surveillance

The AES surveillance integrated with AFP and other vaccine preventable diseases (VPDs) surveillance to ensure that all identified AES case are adequately investigated for laboratory confirmation following all the present procedure of passive surveillance.

6.10.5 Case notification and investigation

Case Notification

All health facilities and/or private practitioners should admit any suspected AES case to the hospital and report immediately to the DSFP (HSO i.e. RMO/RP). HSO will also informs DSFP and SIMO. The DSFP will send the LSO to investigate the case within 48 hours of notification. HSO in consultation with DSFP may assign medical doctor (one or as required) of the facility to expedite investigation of the AES case by filling up AES Case Investigation Form (*Annexure 14*). DSFP also ensure follow-up of laboratory confirmed JE cases six months after the onset to confirm and report the presence or absence of disability and other sequelae.

Case Investigation

Step-1: Assign a case identification number (ID) to the AES case

ID Number is unique and is also called EPID number, which has alpha-numeric coding. Alphabets used are all capital and includes the name of disease under surveillance i.e. AES followed by initial three alphabets of country e.g. BAN for Bangladesh, with a space in between. The alphabetic coding is followed by a series of 4 digits sequences; the first 2 digits encode for the district where the case developed the symptoms, the next 3 digits encode for Upazila/Municipality/City Corporation; the next 2 digits encode for the year of onset and the final 3 digits encode for the AES case serial number for that place during the year of onset.

Example: **AES – BAN - ## - ### - ## - ###**

AES – BAN - 09 - 092 - 16 - 005

AES (Reporting Case), **BAN** (country code), **09** (district code for Sylhet), **092** (upazila code of Zakiganj), **16** (year of onset of AES) and **005** (serial number of AES case with onset in 2016)

Step-2: Mobilize all members of the investigation team and prepare for the investigation

As soon as the DSFP receives the notification of a suspected AES case s/he should immediately contact to LSO and SIMO. The LSO actively participates in every AES case investigation. LSO should bring the following materials to the hospital:

- Investigation Form for Acute Encephalitis Syndrome (AES) (*Annexure 14*)
- CSF/Blood/serum specimen collection kit
- A specimen transport carrier (a vaccine carrier specified for collection and transportation of specimen of AFP/Measles/CRS cases) with 4 frozen icepacks.

SIMO will immediately meet DSFP and LSO and actively participate in AES case investigation/reinvestigation.

Step-3: Investigate the suspected AES case within 48 hours of report and fill in the Case Investigation Form

LSO with SIMO if available jointly should investigate the suspected AES case within 48 hours of the report received by DSFP. If SIMO is not available, LSO should proceed immediately without waiting. If LSO is not available, DSFP should designate any other trained Medical Officer to investigate the case, otherwise will conduct by him/herself. In such event, SIMO should reinvestigate the case as soon as possible.

The investigating team must go to the hospital where the case is admitted. The investigator should carefully obtain the history of illness and conduct physical examination of the patient to verify whether the case meets the AES case definition.

For the confirmed AES case, investigation form *(Annexure 14)* to be filled completely. Coordinate the collection of specimens (CSF and/or serum) and transportation to the designated laboratory.

6.10.6 Specimen collection & handling

Sample (CSF and/or serum) to be collected soon after admission of a patient in the hospital who meets the AES case definition. Cerebrospinal fluid (CSF, most desired) or serum specimen to be referred for detection of IgM antibodies to Japanese Encephalitis Virus.

CSF is an important diagnostic specimen to differentiate bacterial from viral infection and encouraged to send to a competent local laboratory for rapid and appropriate testing for identification of possible other agents of AES (i.e. gram stain, cell count, protein/glucose determination, latex agglutination, bacterial culture, JE IgM).

The majority of JE infections are asymptomatic. Therefore, in areas that are highly endemic for JE, it is possible to have encephalitis due to a cause other than JE virus and have JE virus-specific IgM antibody present in serum. IgM antibody may also be present in serum after JE vaccination. Therefore, testing of a CSF sample for JE and Nipah viruses from all encephalitis cases is recommended.

Cerebrospinal Fluid (CSF)

- The finding of JE IgM in CSF confirms the diagnosis of JE. Hence, CSF sample is the most desired and recommended.
- IgM to JE virus rises earlier in CSF than in serum and rises to higher level in CSF than in serum (2-4 times).
- CSF is the preferred sample for the diagnosis of JE. For this purpose, about 0.5 – 1.0 ml of CSF should be collected in sterile tube/vial.
- CSF is to be transported as soon as possible (ideally within 1 hour) to the laboratory for routine investigations and should not be refrigerated or exposed to extreme cold, excessive heat or sunlight. However, if there is likely to be delay beyond one hour, specimens for virology are to be refrigerated.

- CSF samples for virological testing are to be sent to the JE Lab at IEDCR, Mohakhali, Dhaka, as soon as possible. Before transport to the laboratory, they to be kept at 4°-8°C for 1-3 days or at below -20°C for longer term storage. If the specimens have been frozen, they should be transported frozen. Repeated freezing and thawing of CSF should be avoided as this may lead to instability of IgM antibodies.

Serum

- A JE IgM positive result from the serum of a patient with encephalitis is a good indicator of acute infection (although there is a problem of some cross reactivity with other flaviviruses such as 'dengue').
- A blood specimen to be collected on admission. A second sample may be collected, as decided by the programme, at discharge or on the 10th day of illness or at the time of death.
- Blood samples to be collected by vein puncture and placed in a dry sterile tube/vial. 0.5 – 2.0 ml of blood to be collected from infants less than 1 year of age, 2-3 ml blood in case of children under 5 years old and 5 ml for patient over 5 years.
- Whole blood is allowed to clot at room temperature and then stored in a cold box or refrigerator and maintained at 4°-8°C (and not frozen). Once the clot is formed one can separate the serum from the clotted blood by retracting the clot by a sterile stick followed by centrifugation at 1000g for 20 minutes. *(Note: if there is no centrifuge facility, blood is to be kept in the refrigerator until there is complete retraction of the clot from the serum, but no longer than 24 hours)*
- Carefully remove the serum, avoiding extracting red cells and transfer aseptically to a sterile labeled tube/vial.
- Label tube/vial with EPID of the case, patient's name, specimen type and date of collection. Fill the case investigation form in completely.
- Store the serum at 2°-8°C until it is ready for shipment for a maximum period of 7 days. Separated serum samples are to be shipped on frozen ice packs.
- Serum samples received for IgM analysis are to be tested as soon as possible after receipt in the laboratory. Short-term storage of serum (1-3 days) is to be at 2°-8°C. Longer term storage of serum is to be at or below -20°C. Repeated freezing and thawing of serum is to be avoided as this may lead to instability of antibodies.

Test for Malaria

Testing the presence of malarial antigen in patient's blood, collection of whole blood is recommended in EDTA/CPD. Once the 5 ml of vein puncture blood is collected in syringe, about 70 µl (microliter) of blood (2 drops) from the same syringe is to be put to another tube/vial with EDTA for malaria test. The concerned physician is to perform the test him/herself at bed side or with help from laboratory personnel. The result of malaria RDT is to be noted in the patient's case record and investigation form as well.

Specimen Shipping

1. Specimen/s is/are to be shipped to the JE Lab at IEDCR considering maximum period of storage at specimen appropriate temperature and time.

2. Place specimens in "Zip-lock" plastic bags.
3. Place investigation form in a separate plastic bag and tape to inner top of specimen carrier.
4. Place 4 frozen ice packs in the specimen carrier along the sides and place the "Zip-lock" plastic bags containing specimen in the center of carrier.

Completeness and timeliness of reporting from the reporting units should be regularly monitored. To summarize, the following surveillance activities need to be carried out at the district level:

- Monitoring daily/weekly/monthly surveillance reports of AES/JE cases including "Zero" case reports submitted by different reporting Units.
- Ensuring analysis of AES/JE cases and reconciling data with existing, surveillance systems to identify if there are any outbreaks.
- Ensuring that all data from cases are properly collected, analyzed and interpreted.
- Ensuring that surveillance reports and case investigation data are shared with authorities.
- Supervision and monitoring at all levels would be strengthened for ensuring effective surveillance.

6.10.7 Surveillance, Investigation and Response in outbreak setting

6.10.7.1 Definition of JE Outbreak

An outbreak of JE can be defined as an occurrence of the disease in excess of the expected frequency in a given area among a specific group of people over a particular period of time, or two or more epidemiologically linked cases of the illness in a short period. Major outbreaks of JE occur every 2–15 years in endemic areas, especially in areas with low use of JE vaccine. JE transmission normally intensifies during the rainy season, when vector populations increase[5].

6.10.7.2 Changes to surveillance during an outbreak

Only the first 5–10 cases of an outbreak need to be confirmed through laboratory testing. If an outbreak continues over a protracted period, another 5–10 samples should be collected every two to three months to ensure that the outbreak is still due to JE. If the outbreak is not an expected seasonal outbreak, or there are unusual epidemiological features (such as age distribution of cases not consistent with pattern of JE infection or absence of typical vectors or hosts), testing of CSF is especially important, as an encephalitis outbreak could be due to other etiologies.

6.10.7.3 Procedures in case of Suspected AES Outbreak

The SIMO should work closely with the district level Rapid Response Team (RRT) and respond to any suspected AES outbreak. Whenever the SIMO learns of a suspected outbreak, s/he should collect basic data and notify the DSFP and LSO. The SIMO should verify that the symptoms of suspected cases are compatible with AES.

Once the outbreak is confirmed, CSF and/or serum specimens are to be collected during investigation to confirm that the outbreak is caused by JE via serologic testing. In the initial period of surveillance, it is advised to collect specimens from each symptomatic suspected case. The samples are to be sent to JE lab under reverse cold chain with appropriate labeling of each sample.

6.10.7.4 Determining the Cause of AES Outbreak

After an outbreak has been investigated the surveillance unit should review all reported cases and assign them final classification based either on clinical history/signs or laboratory results. The data should be analyzed to determine why and where the outbreak occurred. These data will help to identify in which age group the susceptible individuals are.

6.10.7.5 Severity, timing and location of Outbreak

The severity of the outbreak can be determined by calculating the hospitalization rate; case fatality rate; age-specific attack rates and age-specific case fatality rates. Construct an epidemic curve, which is a graph showing cases by date of onset or by date of report. This curve helps to demonstrate where and how an outbreak began, how quickly the disease is spreading and the stage of the outbreak (start, middle or ending phase). Cases should be plotted by ward map and residence at the time of onset of illness if possible.

6.10.7.6 Recommended Data Analysis

- Number and incidence of suspected cases by week, month, year, age group and geographical area
- Number and incidence of confirmed cases by week, month, year, age group and geographical area
- JE vaccination coverage by year and geographical location (once JE vaccine is introduced)
- Percentage of cases vaccinated and unvaccinated (once JE vaccine is introduced)
- Suspected and confirmed cases: by age-group, sex and geographic area
- Proportion of AES attributed to JE and diagnostic criteria for the attributions
- Immunization status specific incidence
- Percentage of suspected case with CSF and/or serum specimens
- Percentage of cases with serum 10 or more days after onset of illness (when testing methodology is IgM-capture ELISA)
- Case fatality ratio
- Final classification of all suspected cases

Reporting requirements and recommendations

Aggregate JE case counts (confirmed and probable) to track disease burden are sufficient to identify clusters and monitor trends. Aggregate case counts should be reported at least monthly.

6.10.7.7 Public Health Response

Public health response to JE should include the following

Vaccination: JE vaccination should be integrated into national immunization schedules in all areas where JE is recognized as a public health priority. The value of reactive vaccination campaigns during outbreaks of JE has not been studied. If an outbreak occurs in a country or region where JE vaccination has not been introduced, assess whether it is appropriate to implement an immediate vaccine response, considering factors such as size of the outbreak, timeliness of the response, population affected and programmatic capacity. Due to the need for rapid production of protective antibodies, live attenuated or live recombinant vaccines should be

used. When outbreak response vaccination is conducted, planning for introduction into the routine immunization schedule should follow.

Health education and community involvement: there is a direct relationship between the time lag in onset of symptoms and initiation of medical care. Immediate supportive management of cases reduces fatality considerably.

Interruption of transmission: There is little evidence to support a reduction in JE disease burden from interventions other than vaccination of humans, such as vaccination of pigs, environmental management for vector control, and chemical control of vectors.

6.10.7.8 AES Surveillance Indicators

1. **Surveillance Attribute:** Sensitivity

Indicator: Minimum AES rate per 100,000 population

Target: >2/100,000

Calculation:

$$\frac{\text{\# of AES cases reported}}{\text{Total population}} \times 100{,}000$$

2. **Surveillance Attribute:** Completeness of weekly reporting

Indicator: Proportion of completeness of weekly reporting

Target: ≥90%

Calculation:

$$\frac{\text{Total number of completed weekly report}}{\text{Total number of report to be expected}} \times 100$$

3. **Surveillance Attribute:** Timeliness of weekly reporting

Indicator: Proportion of weekly report received in time

Target: ≥80%

Calculation:

$$\frac{\text{Total number of weekly report received in time}}{\text{Total number of report to be expected}} \times 100$$

4. **Surveillance Attribute:** Timing of sample collection

Indicator: Percentage of serum samples taken within 10 days after onset of illness

Target: ≥80%

Calculation:

$$\frac{\text{Total number of sample collected after 10 days of onset of illness}}{\text{Total number of suspected cases}} \times 100$$

5. **Surveillance Attribute:** Any sample collection

Indicator: Percentage of all suspected cases for which at least 1 specimen was collected

Target: ≥90%

Calculation:

Total number of cases from those at least one sample is collected / Total number of suspected cases	X 100

6. **Surveillance Attribute:** CSF sample collection

Indicator: Percentage of all suspected cases for which CSF specimen was collected

Target: ≥80%

Calculation:

Total number of cases from those at least one sample is collected / Total number of suspected cases	X 100

7. **Surveillance Attribute:** Condition of sample

Indicator: Percentage of CSF/serum samples reaching at laboratory in adequate condition

Target: ≥80%

Calculation:

Total number of samples arriving at national laboratory in adequate condition / Total number of sample arriving at the laboratory	X 100

Adequate means

1) the specimen is transported using reverse cold chain and

2) the sample volume is greater than 100 µL

8. **Surveillance Attribute:** Timeliness of laboratory result

Indicator: Proportion of laboratory results reported <7 days after receipt of sample

Target: ≥80%

Calculation:

Total number of samples with result within 7 days / Total number of samples arriving at the laboratory	X 100

References:

1. *WHO fact-sheets of Japanese-encephalitis*
2. *Yello book, Japanese -encephalitis, CDC, USA*
3. *Surveillance guideline for VPDs -module 9, SEARO, WHO*
4. *https://microbeonline.com/japanese-encephalitis-je-virus-structure-life-cycle-pathogenesis-diagnosis*
5. *WHO Vaccine-Preventable Diseases Surveillance Standards-JE*

7. Diphtheria

7.1 Introduction

Diphtheria is an acute, toxin-mediated disease caused by the bacterium *Corynebacterium diphtheriae*. The name of the disease is derived from the Greek diphthera, meaning leather hide. The disease was described in the 5th century BCE by Hippocrates, and epidemics were described in the 6th century AD by Aetius. The bacterium was first observed in diphtheritic membranes by Klebs in 1883 and cultivated by Loffler in 1884. Antitoxin was invented in the late 19th century, and toxoid was developed in the 1920s.

Diphtheria

The name derived from Greek diphthera means leather hide

Recognized by Hippocrates in 5th century BCE

Epidemics described in 6th century

C. diphtheriae described by Klebs in 1883

Toxoid developed in 1920s

7.2 The causative agent

C. diphtheriae is an aerobic gram-positive bacillus. Toxin production (toxigenicity) occurs only when the bacillus is itself infected (lysogenized) by a specific virus (bacteriophage) carrying the genetic information for the toxin. Only toxigenic strains can cause severe disease. There are 4 biotypes of C. diphtheriae — gravis, mitis, belfanti and intermedius. The most severe disease is associated with the gravis biotype, but any strain may produce toxin. Nontoxigenic strains are increasingly associated with infective endocarditis.

7.3 Pathogenesis

The pathogenesis of diphtheria involves bacterial exotoxin as well as cell wall components, such as the O- and K- antigens. The heat-stable O-antigen is common to all corynebacteria. The heat-labile K-antigen is variable and permits differentiation between individual strains. While the K-antigen is important for mucosal attachment, invasiveness is facilitated by the cord factor, a toxic glycolipid. The most important virulence factor of C. diphtheriae is the exotoxin, a bacteriophage mediated, highly conserved polypeptide encoded by the bacterial chromosome. Outside the host cell, the exotoxin is relatively inactive, but following cellular attachment and internalization by its non-toxic fragment B, a highly toxic fragment (A) is detached that kills cells through inhibition of cellular protein synthesis. Diphtheria exotoxin causes both local and systemic cell destruction[2].

7.4 Communicability

Transmission may occur as long as virulent organisms are viable. A case usually remains infectious for a period of 2-4 weeks, but chronic carriers may shed the organism for 6 months or more.

Transmission

Transmission is most often person-to-person spread from the respiratory tract through droplets or direct contact with respiratory secretions. Rarely, transmission may occur from skin lesions or articles soiled with discharges from lesions of infected persons (fomites). The incubation period of diphtheria is 2–5 days (range, 1–10 days).

A person is infectious as long as virulent bacilli are present in discharges and lesions. The period of infectivity is variable, but organisms usually persist 2 weeks, and seldom more than 4 weeks, without antibiotics. Chronic carriers may shed organisms for 6 months or more. Effective antibiotic therapy promptly terminates shedding.

7.5 Reservoir

Humans are the only known reservoir of C. diphtheriae. In most cases, transmission of C. diphtheriae to susceptible individuals results in transient pharyngeal carriage rather than in disease. During outbreaks, high percentages of children are found to be transient carriers.

7.6 Occurrence

The disease has almost disappeared from the developed countries as a result of high immunization coverage. Continued foci of epidemicity and endemicity exist in some parts of the world with low-immunization coverage, including the Indian subcontinent and south East Asia[2].

7.7 Clinical Features

Diphtheria can involve almost any mucous membrane. For clinical purposes, it is convenient to classify diphtheria into different types depending on the site of disease.

Clinical features

Incubation period 2-5 days (range, 1-10 days)

May involve any mucous membrane

Classified based on site of disease

- anterior nasal
- pharyngeal and tonsillar
- laryngeal
- cutaneous
- ocular
- genital

Pharyngeal and Tonsillar Diphtheria

- Insidious onset of pharyngitis
- Within 2-3 days membrane forms
- Membrane may cause respiratory obstruction
- Fever usually not high but patient appears toxic

Anterior Nasal Diphtheria

The onset of anterior nasal diphtheria is indistinguishable from that of the common cold and is characterized by a mucopurulent nasal discharge, sometimes may become blood-tinged. A white membrane usually forms on the nasal septum. Due to poor systemic absorption of toxin in this location the disease is usually very mild and can be terminated rapidly by antitoxin and antibiotic therapy.

Pharyngeal and Tonsillar Diphtheria

Pharynx and the tonsils are the most common sites of diphtheria infection. These sites are usually associated with substantial systemic absorption of toxin.

Early symptoms include malaise, sore throat, anorexia and low-grade fever. Within 2–3 days, a bluish-white membrane forms and extends, varying in size covering from a small patch on the tonsils to most of the soft palate. The membrane becomes greyish-green in color or black if bleeding occurs. There is a minimal amount of mucosal erythema surrounding the membrane. The membrane is adherent to the tissue and forcible attempts to remove it cause bleeding. Extensive membrane formation may result in respiratory obstruction.

The patient may recover at this point; or if enough toxins are absorbed, severe prostration may develop with pallor, rapid pulse, stupor, coma and may lead to death within 6 to 10 days. Fever

is usually not high, even though the patient may appear toxic. Patients with severe disease may develop marked edema of the submandibular areas and the anterior neck along with lymphadenopathy, giving a characteristic "bullneck" appearance.

Laryngeal Diphtheria

Laryngeal diphtheria can be either an extension of the pharyngeal form or the only site involved. Symptoms include fever, hoarseness and a barking cough. The membrane can lead to airway obstruction, coma and death.

Cutaneous Diphtheria

Skin infections may be manifested by a scaling rash or by ulcers with clearly demarcated edges and membrane, but any chronic skin lesion may harbor C. diphtheriae, along with other organisms. Cutaneous diphtheria is not reportable Disease.

7.8 Complications

The most frequent complications of diphtheria are myocarditis and neuritis. Myocarditis may present as arrhythmia, can occur early in the course of the illness or weeks later sometimes causes heart failure even death.

Complication
Most attributable to toxin
Severity generally related to extent of local disease
Most frequent complications are myocarditis and neuritis
Death occurs in 5%-10%

Neuritis most often affects motor nerves and usually resolves completely. Paralysis of the soft palate is most frequent during the third week of illness. Eye muscles, limbs and diaphragm paralysis can occur after the fifth week. Secondary pneumonia and respiratory failure may result from diaphragmatic paralysis. Other complications include otitis media and respiratory insufficiency due to airway obstruction, especially in infants.

Death

Case-fatality rate for diphtheria is 5%–10%, higher death rates (up to 20%) can occur in persons <5 and >40 years of age.

7.9 Laboratory diagnosis

Gram stain

Diagnosis of diphtheria based upon direct microscopy of smear is not advisable as false positives and false negatives may occur.

Culture

The clinical specimen for culture should be taken from nose, throat or diphtheritic membrane. C. diphtheriae requires special culture media containing tellurite to grow and forms grey to black colonies. The four biotypes (intermedius, belfanti, mitis or gravis) of C. diphtheriae can be distinguished by colonial morphology and biotyping. Certain biochemical tests are required to differentiate pathogenic C. diphtheriae from corynebactria of the normal flora (diphtheroids) in the throat.

Toxigenicity test

All isolates of C. diphtheriae should be subjected to toxigenicity testing to determine the production of diphtheria toxin. Toxigenicity testing can be done by Elek test or PCR. Elek test is based on the double diffusion of diphtheria toxin and antitoxin in an agar medium. The production of diphtheria toxin can be detected within 18 to 48 hours by the formation of a toxin-antitoxin precipitin band in the agar. Demonstration of toxin production confirms a case as diphtheria.

Polymerase chain reaction (PCR) test

Isolation of C. diphtheriae may not always be possible because many patients will have received antibiotics before a diagnosis of diphtheria is considered. PCR allows for detection of the regulatory gene for toxin production (dtxR) and the diphtheria toxin gene (tox) in nonviable organisms. PCR can be done directly on swab material to detect the presence of the A and B subunits of the diphtheria toxin gene (tox). However, in some cases the presence of tox does not confirm production of toxin; positive PCR results should therefore always be confirmed with the Elek test if there is an isolate. PCR is only available in some reference laboratories and should not replace bacterial culture as the primary and gold standard diagnostic test. However, in some situations (for example, specimens taken post-antibiotics, poor specimen quality or delayed testing due to transportation delays), PCR can be positive and culture negative. These cases should be reviewed to determine their classification

7.10 Treatment

Has three main components:

Administration of diphtheria antitoxin

The mainstay of treatment is intramuscular or intravenous administration of diphtheria antitoxin (a hyper immune anti-serum produced in horses) to neutralize circulating toxin before it reaches target cells. Early administration after testing for hypersensitivity is essential as it can neutralize only free toxin.

The minimum therapeutic dose is unknown; recommendations are based on clinical experience and the assumption that duration of disease and extent of membrane formation indicate the toxin burden. As a guide, doses range from 10,000 units in tonsillar diphtheria of short duration, to 40,000–60,000 units in pharyngeal disease, to 100,000–150,000 units in extensive disease of 3 or more days' duration.

Recommendations differ on the route of administration (intramuscular vs intravenous), but in severe disease at least some of the dose should be administered intravenously.

Antibiotic therapy

Antibiotics have no impact on already established toxin induced lesions but limit further bacterial growth and the duration of corynebacterial carriage that often persists even after clinical recovery. Penicillin, 0.6–1.2 gm every 6 hours, or erythromycin, 0.5 gm every 6 hours, is recommended. Antibiotic therapy should be continued for 14 days.

Supportive measures

Supportive management of complications, with particular attention to the airway and cardiac manifestations are an important part of case management. Patients should be nursed in strict isolation and should be attended by staff with documented immunization histories.

Early in the illness, respiratory and cardiac complications are the greatest threat. These can be minimized by close monitoring (including regular ECG) and early intervention (e.g. pacing for conduction disturbances, drugs for arrhythmias). Some experts recommend tracheostomy or intubation at an early stage to ensure continued patency of a compromised or potentially compromised airway, and mechanical removal of any tracheobronchial membrane

7.11 Prevention

Prevention is best achieved by a primary series of 3-dose diphtheria toxoid-containing vaccine, recommended with the first dose administered as early as 6 weeks of age. Subsequent doses should be given with an interval of at least 4 weeks between doses. The third dose of the primary series should be completed by 6 months of age if possible. Immunization programmes should ensure that 3 booster doses of diphtheria toxoid-containing vaccine are provided during childhood and adolescence. The diphtheria booster doses should be given in combination with tetanus toxoid using the schedule of i.e. at 12–23 months of age, 4–7 years of age, and 9–15 years of age, using age-appropriate vaccine formulations.

Diphtheria infection does not always confer protective immunity. Individuals recovering from the disease should therefore complete active immunization by receiving an age appropriate booster dose of diphtheria toxoid, or a full primary series if indicated during convalescence.

For close contacts of diphtheria, a diphtheria booster, appropriate for age, should be given. Contacts should also receive antibiotic as prophylaxis. Close contacts are considered to be household members and others with a history of direct contact with a case. These may include caretakers, relatives, sexual contacts, fellow students and friends who regularly visit the home. Medical staff exposed to the case's oral or respiratory secretions or exposed to their wound should also be monitored. Ideally, surveillance staff should communicate daily with contacts to monitor for new symptoms.

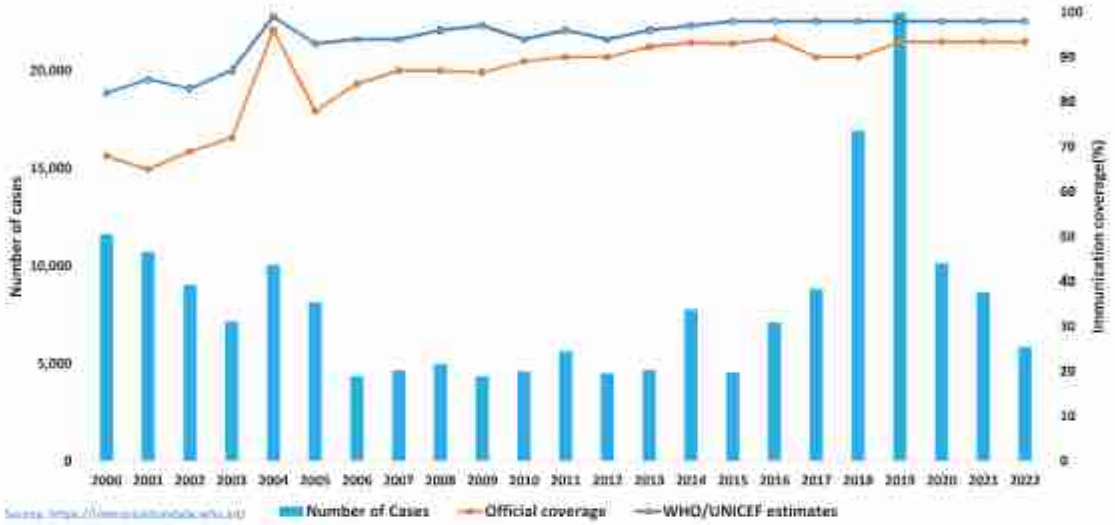
Contacts of cutaneous diphtheria should be treated as described above; however, if the strain is shown to be nontoxigenic, investigation of contacts should be discontinued.

7.12 Diphtheria Surveillance

Diphtheria remains an important public health problem in many parts of the world. Diphtheria was one of the most common causes of death among children in the pre-vaccine era. Before the introduction of diphtheria toxoid in 1920s and 1930s, diphtheria was largely a disease of children, affecting 10% of this population with a case fatality rate of 30-40%. During the past decade, many developing countries have achieved marked reduction in diphtheria incidence with high childhood immunization coverage. The use of diphtheria antitoxin has reduced case fatality rates to 5-10%, and widespread use of DTwP/DTaP vaccine or pentavalent vaccine and booster doses of Td have reduced the number of diphtheria cases. The largest outbreak of the recent past was

reported from the Russian Federation and former Soviet Republics in the 1990s. More than 157,000 cases and 5,000 deaths were reported during 1990–1998. In the period 2011–2015, India had the largest total number of reported cases each year, with a 5-year total of 18,350 cases, followed by Indonesia and Madagascar with 3,203 and 1,633 reported cases respectively. The South-East Asia Region was the source of 55–99% of all reported cases each year during this period. Only 53 diphtheria cases were reported in the United States from 1980- 2001 and 77% of these were ≤ 15 years of age.

Figure 27: Global annual reported cases with DPT3 coverage 2000-2022



However, sporadic cases and outbreaks still occur in different countries among population subgroups. A feature of these outbreaks is that the majority of cases have occurred among adolescents and adults instead of children. Rarely, outbreaks occur in well-vaccinated populations with intense exposure to toxigenic C. diphtheriae, but disease is usually mild, with fewer complications and no fatalities.

7.12.1 Diphtheria surveillance in Bangladesh

In 2007, total 86 cases reported through AFP and EPI diseases surveillance network in Bangladesh and 20% of these cases were less than 5 years of age. Following influx of forcibly displaced Myanmar nationals (FDMN) into Cox's Bazar district in Bangladesh, as on 18 June 2018, total 7 823 diphtheria case-patients were reported through EWARS, including 243 case-patients who were tested positive on PCR. Among them, total number of deaths is 43 (case-fatality proportion <1.0%). On the other hand, in 2018, 35 cases of suspected diphtheria reported among Bangladeshi community. In 2019, the number of suspected diphtheria cases dropped down to 14 and only 10 cases in 2020. In 2022, only three diphtheria cases were reported among Bangladeshi community.

Table 14: Suspected diphtheria cases, by Age and sex, Bangladesh 2010-2022

Cases by Sex	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Male	14	5	10	2	6	3	1	2	19				3
Female	13	6	6	2	7	3	1	3	16				3
Diphtheria Total	27	11	16	4	13	6	2	5	35	14	10	0	6

Cases by Age	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
0-11 Months				2	2	1				1			
1-4 years	8	4	6	1	1		1	1	2	1			
5-9 years	6	3	2	1	1	3		1	5	1			2
10-14 years	2	1	2		2	1	1	1	16	2			3
15+ years	11	3	6		7	1		2	12	9			1
Diphtheria Total	27	11	16	4	13	6	2	5	35	14	10	0	6

7.12.2 Rational and Objectives of Surveillance

- Monitor disease burden and define transmission patterns
- Determine appropriate vaccine policy such as to introduce booster doses or change the vaccine formulation.

7.12.3 Case definition and final classification

Suspected case

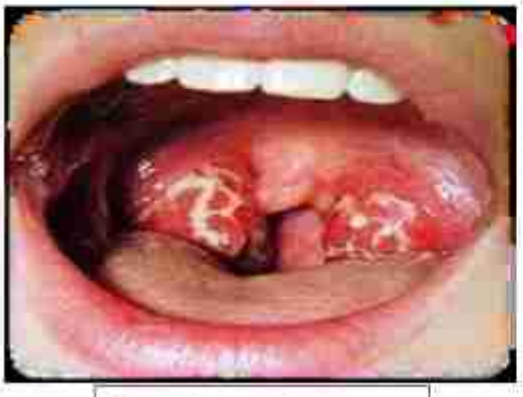
An illness of the upper respiratory tract characterized by the following:

pharyngitis, nasopharyngitis, tonsillitis or laryngitis (Sore throat) and fever

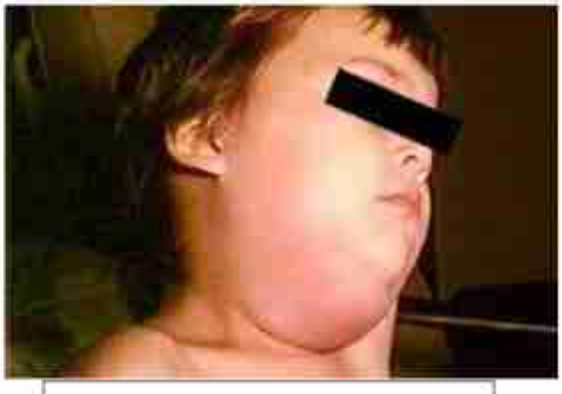
and adherent pseudomembrane of the pharynx, tonsils, larynx and/or nose and without other apparent cause determined by the physician

A diphtheria pseudomembrane is an exudate that is greyish, thick, firmly adherent and patchy to confluent. Dislodging the pseudomembrane is likely to cause profuse bleeding.

Symptoms of suspected diphtheria



Pseudomembrane



Bull neck

Case classification

Laboratory-confirmed case4

A laboratory-confirmed case is a person with Corynebacterium spp. isolated by culture and positive for toxin production, regardless of symptoms. Toxigenicity must be confirmed by the phenotypic Elek test in all instances. Polymerase chain reaction (PCR) can complement surveillance and may qualify as laboratory confirmed after reviewing the epidemiology and clinical manifestations of the case.

Laboratory confirmed cases may be further classified into three subcategories based on the type of surveillance occurring in the country.

1. *Laboratory-confirmed classic respiratory diphtheria* cases meet the suspected case definition and are laboratory-confirmed as defined above.
2. *Laboratory-confirmed mild respiratory/ asymptomatic diphtheria* cases have some respiratory symptoms such as pharyngitis and tonsillitis, but no pseudomembrane, or no symptoms (usually identified via contact tracing).
3. *Non-respiratory laboratory-confirmed diphtheria* cases have a skin lesion or non-respiratory mucosal infection (for example, eye, ear or genitalia) from which Corynebacterium spp. is isolated by culture and tests positive for toxin production.

Epidemiologically linked case

An epidemiologically linked case meets the definition of a suspected case and is linked epidemiologically to a laboratory confirmed case. In this situation, a person has had intimate respiratory or physical contact with a laboratory-confirmed case within the 14 days prior to onset of sore throat.

Clinically compatible case

This type of case meets the definition of a suspected case and lacks both a confirmatory laboratory test result and epidemiologic linkage to a laboratory-confirmed case.

Discarded case

A discarded case is a suspected case that meets either of these criteria:

Corynebacterium spp. but negative Elek test (nontoxigenic Corynebacterium) OR

negative PCR for the diphtheria toxin (tox) gene.

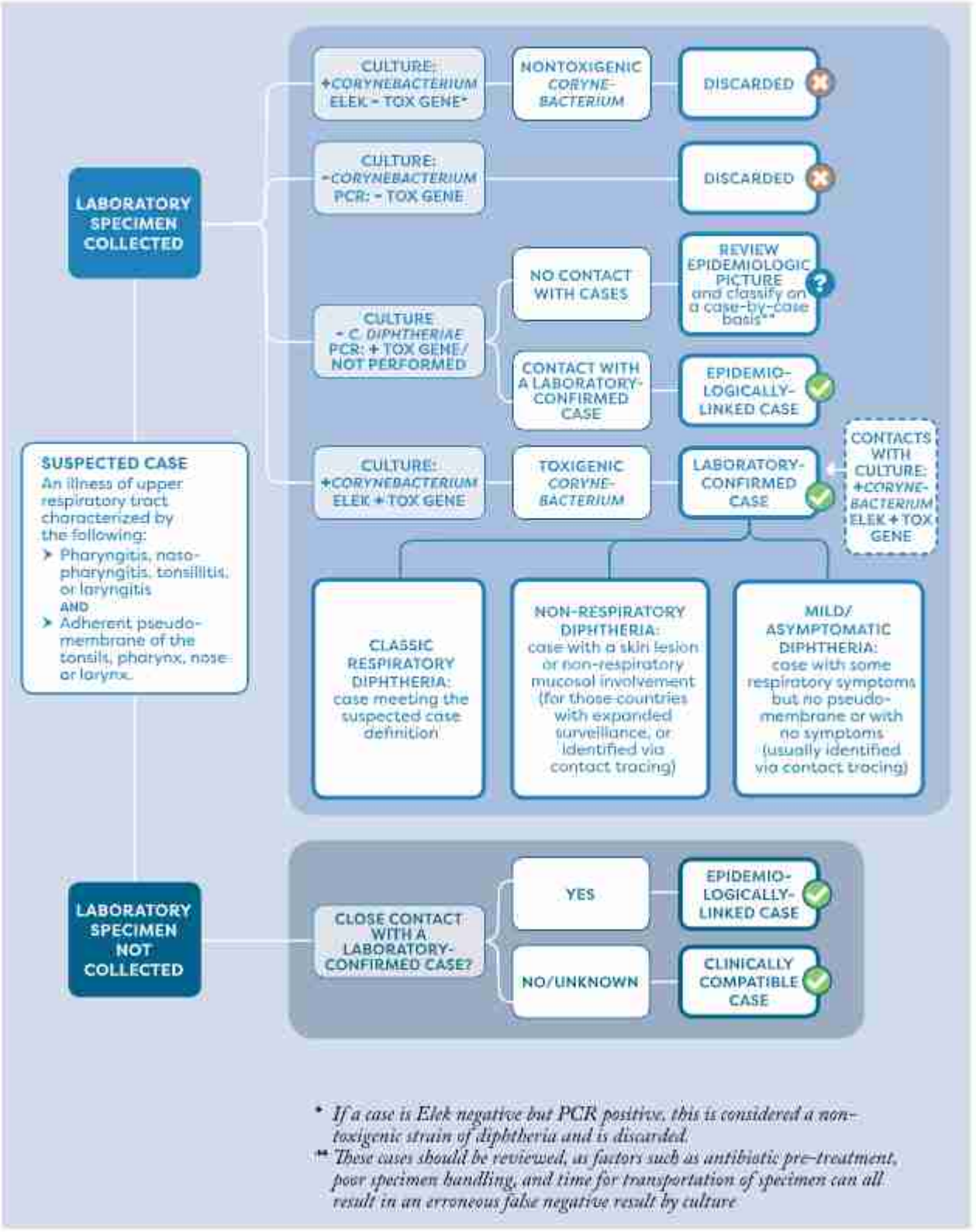
Classifying asymptomatic or mild cases

Sometimes during outbreak investigations in which household contacts are investigated, a person may be identified with Corynebacterium and have evidence of toxigenicity but does not meet the suspected case definition because the person is asymptomatic or has only mild disease. These persons should still be reported as laboratory-confirmed cases, as their treatment and public health response is the same as other laboratory-confirmed cases.

7.12.4 Diphtheria Outbreak

Two temporally and geographically linked cases, of which at least one is laboratory-confirmed, is considered an outbreak of diphtheria.

Figure 28: Final case classification of Diphtheria



* *If a case is Elek negative but PCR positive, this is considered a non-toxigenic strain of diphtheria and is discarded.*

** *These cases should be reviewed, as factors such as antibiotic pre-treatment, poor specimen handling, and time for transportation of specimen can all result in an erroneous false negative result by culture.*

7.12.4.1 Case notification

Reporting of all respiratory diphtheria case should be done by attending physician of the hospital/clinic through AFP and EPI disease report form. The filled-up report form should be submitted to Hospital Surveillance Officer on the same day. HSO should include the data of the case in the weekly line listing form and send to the DSFP.

All suspected cases of diphtheria should be immediately reported Disease Surveillance Focal Person/s (Civil Surgeon, Chief Health Officer/CC, UHFPO) and Programme Manager, EPI. Cluster of diphtheria cases during the same time period and from the same geographic area would suggest a diphtheria outbreak. Hence timely reporting of individual cases of diphtheria is important

7.12.4.2 Case Investigation

A clinician should notify HSO/LSO of any suspected diphtheria case immediately in order to arrange for DAT to be given to the case. HSO/SIMO should investigate the case by using Diphtheria CIF (*Annexure 15*) within 48 hours of report regardless of the case's vaccination status. With case-based surveillance, a case investigation form should be completed for every case and close contacts identified. All suspected diphtheria cases should be isolated and have two specimens collected (pharyngeal swab over and around edges of pseudomembrane) prior to antibiotic treatment. Cases should then be treated promptly without waiting for laboratory confirmation.

7.12.4.3 Specimen Collection

Two samples should be collected from every suspected case at first contact:

Condition	Requirements
Window period from onset of symptoms	0 day-2 weeks, efforts should be made to collect specimen before initiation of antibiotic therapy
Type of specimen	Throat swab or pieces of membrane
Number	2 in duo swab, if duo swab not available then 1 swab
Transport media	Silica gel/Amies transport media, plain or with charcoal
Storage and transportation conditions	2–8°C

7.12.4.3.1 Procedures for collecting samples

Material required:

1. Wooden sticks (disposable tongue depressors)
2. Gloves
3. Surgical mask
4. Face shield or goggles

5. Disposable gown
6. Disposable bag
7. Tissues
8. Duo throat swab
9. Amies transport media: plain or with charcoal
10. Zip lock bag
11. Indelible ink pen
12. Laboratory request form (*Annexure 16*)

Throat swab specimen collection

1. Use throat swab made up of cotton, polyester or Dacron.
2. Label the specimen tube with the unique identification code, patient's name and date of collection.
3. Check the expiry date on the tube and transport media to ensure acceptability of the material to be used for sample collection.
4. Put on a surgical mask, eye protection (face shield or goggles), a disposable gown and a pair of gloves.
5. Swab the inflamed area of tonsils, and posterior pharynx, the junction of membrane and mucosal lining is the best site for specimen collection. If membrane is visible, then rub the swab beneath the membrane with care. Do not try to dislodge the membrane as it may lead to bleeding.
6. Piece of membrane can also be collected on the swab.
7. Immediately place the throat swab sample in Amies transport media till the bottom of the media.
    a. if capped swab, then throw the cap of the tube.
    b. if un capped swab – then cut the shaft of the swab to fit into the tube and cap it securely.
8. Take off the gloves, gown, eye protection and mask in an appropriate order and perform hand hygiene.
9. Secure the throat swab in Zip Lock bag and laboratory request form in the space provided outside the bag.
10. Fill the laboratory request form *(Annexure 16).*
11. Ship the specimen at 4°-8°C to JE lab, IEDCR, Dhaka.

Packing throat swab in silica gel

- Procedure to use silica gel sachet:
  - cut open the silica gel packet from the top
  - ensure that the colour of granules inside the packet is blue. If the colour of granules has turned pink, then it is not fit for use. Open another sachet.
  - now place the loaded throat swab inside the silica gel sachet as shown in the diagram below
  - fold the top end and secure the opening with cello tape

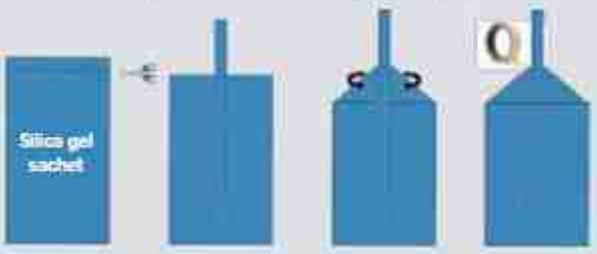


Figure: Packing throat swab in silica gel sachet for transportation to laboratory

Throat swab by Amies transport media

- Depress the tongue with a tongue depressor
- Introduce the swab between the tonsillar pillars and behind the uvula without touching the lateral walls of the buccal cavity
- Swab back and forth across the posterior pharynx
- Any exudates or membrane should be taken for specimen

7.12.4.4 Public Health Intervention

Active case search in community

Active case search (ACS) in the community is very important as there is a probability of finding additional cases among contacts of diphtheria cases.

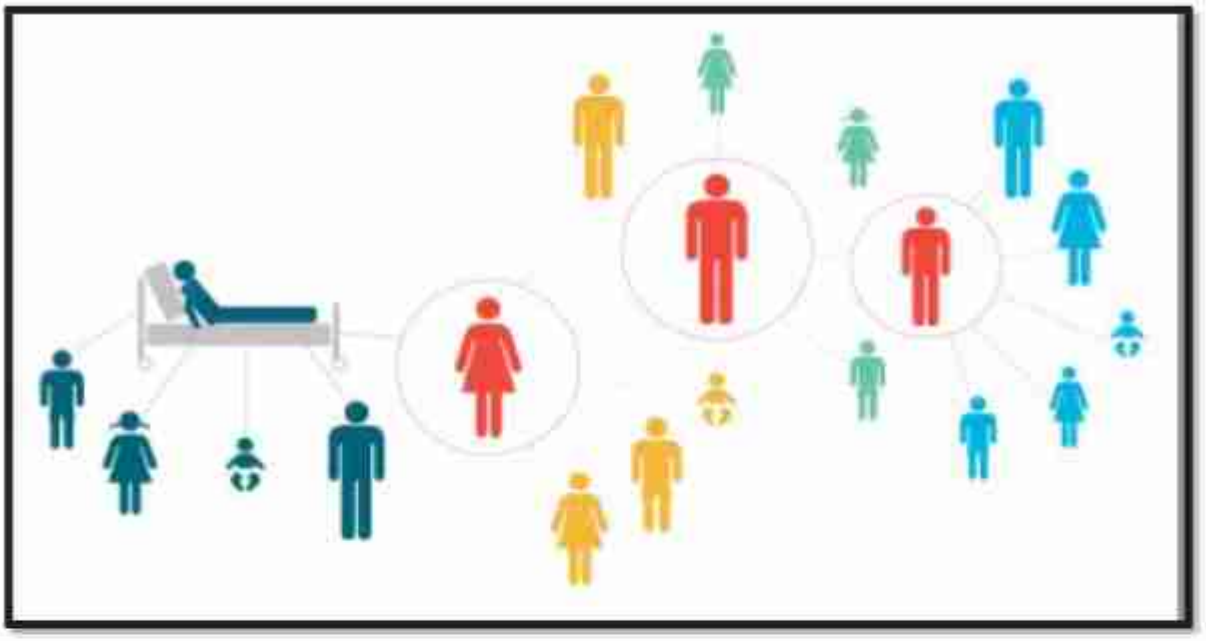
1. ACS should be conducted soon after identification of suspected case preferably within 48 hours of case confirmation.
2. conduct active case search in households, neighborhood, the workplace or school.
3. An assessment of immunization status of the community should also be conducted during active case search in the community.

Contact tracing

Contact tracing of every close contact of index/source case *(annexure 17)* is essential to control and stop the outbreak.

- Contacts are those who have slept under the same roof during the five days prior to the onset and or during the illness. The contact also includes visitors who visited the family and spent >1 hour interacting with the source case and fellow students and care taker(s) if the case was at child friendly center.
- Collect contact information: names, age, mobile telephone number if possible and ways to follow up (telephone, visits).
- Inform the contacts about the outbreak and the disease.
- Assess diphtheria toxoid vaccination status of exposed close contacts and vaccinate if unvaccinated.

Figure 29: Pictorial diagram showing transmission chain through contacts



Chemoprophylaxis of contacts

Choose one of the antibiotics for prevention

IM Benzathine penicillin: a single dose

For children aged ≤5 years: administer 600,000 units.

For those >5 years: administer 1,200,000 units.

Or

Oral erythromycin

For children: 40mg/kg/day, administered in divided dose, 10mg per dose, every 6 hours.

For adults: 1g/day for adults, administered in divided dose, 250mg per dose every 6 hours.

Treat for total 7 days.

Or

Oral Azithromycin

Children: 20mg/kg once daily, to a max of 500mg/day

Adults: 500mg once daily.

Treat for total 3 days.

Contacts must be followed-up on Day 4 and Day 8 for chemoprophylaxis compliance and detection of additional cases.

- Exclude from school or work until 48 hours of antibiotics have been completed.

- Self-assess for signs and symptoms of diphtheria for at least 7 days.
- If person develops any symptom of respiratory tract infection, then seek treatment at a health center immediately.

Vaccination of contacts

All close contacts of suspected diphtheria cases irrespective of age and the healthcare workers in contact to the case should be vaccinated *(annexure 18 & 19)*.

(1) 6 weeks to 6 years: DPT or Pentavalent vaccine (DPT-hepB-Hib).

(2) 7 years and above: Td vaccine.

(3) Pregnant women: Td instead of TT.

- Only one dose of vaccine should be provided if documentary evidence of having completed primary vaccination available. If no documented evidence, provide 3 doses at least 4 weeks interval between each dose.
- Keep record of vaccination of contacts.
- During the subsequent follow up of the contacts on day 4 and day 8, the contact tracing team.
- should check the vaccination card of each contact to confirm whether all contacts have received the vaccine.

Catch-up vaccination

During active case search in the community the RRT should also assess vaccination status of the community where diphtheria case lives. If the vaccination status is poor and significant number of children are unvaccinated at a catchup vaccination could be conducted. The extent/area for vaccination should be decided based on epidemiology, vaccination status, crowding, mobility and other factors at local level.

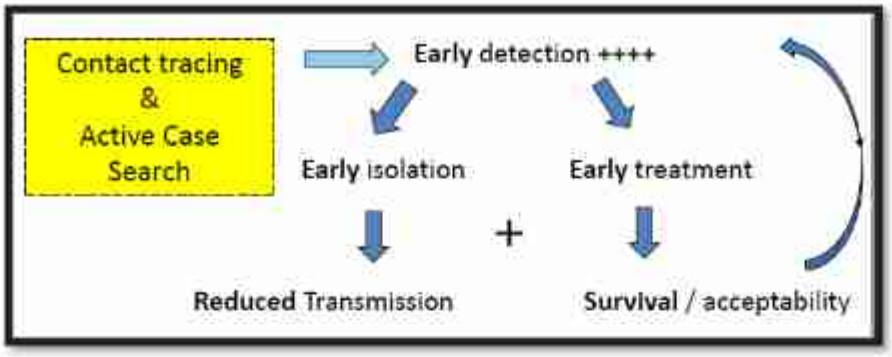
1) 6 weeks to 6 years: DPT or Pentavalent vaccine (DPT-hepB-Hib)
2) 7 years and above: Td vaccine
3) Pregnant women: Td instead of TT

Breaking of Transmission Chain in Diphtheria Infection

It is an active surveillance to break transmission chain by early detection of new cases for treatment and isolation. At the same time, effective contact tracing, looking for sign-symptoms among those identified contacts (as per case definition of contact), ensuring chemo-prophylaxis and vaccination of the contacts including follow-up is equally important.

Active Case Search should be conducted within around neighbouring households in the community with carefully collected travel history of the case at least 5 days prior (incubation period) and 2 weeks after to onset of illness (period of infectivity) if not isolated and have not completed at least 48 hours of antibiotic treatment.

Role of Contact Tracing and Active Case Search to STOP Transmission Chain



If the source case or suspected case/s identified during "Active Contact and Case Search" in the community, have visited any Health Facilities for this illness or any community for whatever the reason might be, additional case should be searched for at those Health Facilities and Communities.

Intervention during an outbreak

During outbreaks, additional cases using clinical diagnosis based on typical pseudomembraneous pharyngitis without laboratory confirmation is an good option. However, laboratory investigation of suspected cases is strongly recommended. Do not delay treatment pending laboratory confirmation. Depending on the size of the outbreak RRT may choose to not test all suspected cases, to avoid overwhelming the laboratory. In this situation, the definition of an epidemiologically linked case can be extended to include linkage to another epidemiologically linked case, rather than to a laboratory-confirmed case. This chain should only continue for approximately two to three incubation periods (about three weeks), at which point any new cases identified should be tested to confirm the outbreak continues to be toxigenic diphtheria. Once five cases are confirmed to be toxigenic diphtheria, epidemiological linking to other epidemiologically linked cases can continue. The process of reconfirming diphtheria among new cases should continue every two to three incubation periods. Cases should be line listed.

Additionally, for outbreaks lasting for an extended period, at least 5 samples should be tested by culture and Elek every month among suspected cases with no epidemiologic link to a PCR-confirmed case. This helps to balance the limited resources during an outbreak[4].

7.12.5 Diphtheria Surveillance performance indicators

1. **Surveillance Attribute:** Completeness of reporting

Indicator: Proportion of surveillance units sending diphtheria report, including 'zero-reporting' to the national level on time

Target: ≥90%

Calculation: Completeness of reporting

$$\frac{\text{Surveillance units reporting diphtheria data to the national level}}{\text{Total number of surveillance units}} \times 100$$

2. Surveillance Attribute: Timeliness of reporting

Indicator: Proportion of surveillance units sending diphtheria reports, including 'zero-reporting' to the national level on time

Target: ≥80%

Calculation: Timeliness of reporting

$$\frac{\text{Surveillance units reporting diphtheria data to the national level on time}}{\text{Total number of surveillance units}} \times 100$$

3. Surveillance Attribute: Timeliness of investigation

Indicator: Proportion of all suspected cases investigation initiated within 48 hours of notification

Target: ≥80%

Calculation:

$$\frac{\text{Number of suspected cases investigation initiated within 48 hours of notification}}{\text{Total number of suspected cases}} \times 100$$

4. Surveillance Attribute: Specimen collection

Indicator: Proportion of suspected diphtheria cases with two specimens collected

Target: ≥80%

Calculation:

$$\frac{\text{Number of suspected cases of diphtheria with 2 specimens collected}}{\text{Total number of suspected cases}} \times 100$$

5. Surveillance Attribute: Timeliness of Specimen collection

Indicator: Percentage of suspected diphtheria cases with specimens taken before antibiotic administration

Target: ≥80%

Calculation:

$$\frac{\text{Number of cases with specimens taken before antibiotic administration}}{\text{Total number of suspected cases}} \times 100$$

6. Surveillance Attribute: Adequacy of investigation

Indicator: Proportion of all suspected diphtheria cases that have had an adequate investigation

Target: ≥80%

Calculation:

$$\frac{\text{Number of suspected cases with adequate investigation}}{\text{Total number of suspected cases}} \times 100$$

Note :

- Adequate investigations include completing a case investigation form, collecting specimen for lab confirmation, line listing of close contacts.

For any case, if any of the above are not conducted, the investigation will be considered inadequate.

7. **Surveillance Attribute:** Timeliness of specimen transport

Indicator: Proportion of specimens received at the laboratory within 2 days of collection

Target: ≥80%

Calculation:

$$\frac{\text{Number of specimens received within 2 days of collection by laboratory}}{\text{Number of specimens received}} \times 100$$

8. **Surveillance Attribute:** Toxigenicity testing rate

Indicator: Proportion of specimens tested for toxigenicity by Elek testing

Target: ≥80%

Calculation:

$$\frac{\text{Number of specimens tested for toxigenicity by Elek testing}}{\text{Number of specimens received}} \times 100$$

9. **Surveillance Attribute:** Timeliness of laboratory result

Indicator: Proportion of specimens tested by culture with results reported within 3 days of receipt of specimen

Target: ≥80%

Calculation:

$$\frac{\text{Number of specimens tested by culture with results reported within 3 days of specimen receipt}}{\text{Number of specimens tested by culture}} \times 100$$

References:

1. *Epidemiology and Prevention of Vaccine-Preventable Diseases-Diphtheria, CDC, USA*
2. *Surveillance Guide for Vaccine-Preventable Diseases in the WHO South-East Asia Region, module 4, Diphtheria*
3. *https://www.who.int/immunization/monitoring_surveillance/burden/vpd/surveillance_type/passive/diphtheria/en/*
4. *WHO Vaccine-Preventable Diseases Surveillance Standards-Diphtheria*

8. Pertussis

8.1 Introduction

Pertussis or whooping cough is an acute infectious disease caused by the bacterium Bordetella pertussis. In the 20th century, pertussis was one of the most common childhood diseases and a major cause of childhood mortality. It is an endemic disease common to children (especially young children) everywhere, regardless of ethnicity, climate or geographic location. Outbreaks of pertussis were first described in the 16th century, and the organism was first isolated in 1906. Before the availability of pertussis vaccine in the 1940s, more than 200,000 cases of pertussis were reported annually. Since widespread use of the vaccine began, incidence has decreased more than 80% compared with the pre-vaccine era. . The recent epidemics of pertussis in several high-income countries has indicated waning of immunity following acellular pertussis vaccine and the need for additional booster doses for better disease control.

Pertussis

Acute infectious disease caused by Bordetella pertussis

Outbreaks first described in 16th century

Bordetella pertussis isolated in 1906

Estimated 195,000 deaths worldwide in 2008

Estimated 24.1 million pertussis cases and 160 700 deaths from pertussis in children < 5 years of age in 2014

8.2 Causative Agent

Bordetella pertussis

Fastidious gram-negative bacteria

Antigenic and biologically active components:

- pertussis toxin (PT)
- filamentous hemagglutinin (FHA)
- agglutinogens

adenylate cyclase

- pertactin
- tracheal cytotoxin

B. pertussis is a small, aerobic gram-negative rod. It is fastidious and requires special media for isolation, produces multiple antigenic and biologically active products responsible for the clinical features; these are pertussis toxin, filamentous hemagglutinin, agglutinogens, adenylate cyclase, pertactin and tracheal cytotoxin.

8.3 Pathogenesis

Pertussis is primarily a toxin-mediated disease. The bacteria attach to the cilia of the respiratory epithelial cells, produce toxins that paralyze the cilia, and cause inflammation of the respiratory tract, which interferes with the clearing of pulmonary secretions. Pertussis antigens appear to allow the organism to evade host defenses, in that lymphocytosis is promoted but chemotaxis is impaired. Until recently it was thought that *B. pertussis* did not invade the tissues. However, recent studies have shown the bacteria to be present in alveolar macrophages.

8.4 Reservoir

Pertussis is a human disease. No animal or insect source or vector is known to exist. Adolescents and adults are an important reservoir for *B. pertussis* and are often the source of infection for infants.

8.5 Transmission

Transmission most commonly occurs by the respiratory route through contact with respiratory droplets, or by contact with airborne droplets of respiratory secretions. Transmission occurs less frequently by contact with freshly contaminated articles of an infected person.

8.6 Communicability

Pertussis is highly communicable in the early catarrhal stage. Thereafter, communicability gradually decreases and becomes negligible in about 3 weeks, despite persisting spasmodic cough with "whoop". When treated with erythromycin, the period of infectivity is usually 5 days or less after onset of therapy.

8.7 Susceptibility and resistance

Susceptibility of non-immunized individuals is universal. Trans-placental immunity in infants has not been demonstrated. One attack usually confers prolonged immunity, although second attacks (some of which may be by B. parapertussis) can occasionally occur.

8.8 Clinical Features

The incubation period of pertussis is commonly 7–10 days, with a range of 4–21 days and rarely may be as long as 42 days.

The illness begins less dramatically with non-specific symptoms and then progresses in the following three stages.

1. Catarrhal: Initially patients develop catarrhal symptoms, including cough. Other nonspecific symptoms are rhinorrhoea, sore throat and conjunctivitis. This stage typically lasts 2 weeks. Fever is present in less than 20% cases.

2. Spasmodic: Later, during the course of 1–2 weeks, coughing paroxysms ending in characteristic whoop occur. In typical cases, cough is frequently followed by vomiting. Paroxysms can occur more than 30 times per 24 hours and are more common at night. They occur spontaneously or are precipitated by external stimuli, such as noise and cold air. Between coughing episodes, there are few clinical signs unless complications develop. This stage also typically lasts 2 weeks.

Clinical Features

- **Infants**
  - Apnoea, cough (no whoop), cyanotic episodes, vomiting, poor feeding, fever, seizures, sudden infant death syndrome
- **Partially immunized**
  - Duration of catarrhal phase may be reduced
  - Whoop may not occur
- **Adults**
  - Prolonged cough, paroxysmal cough, whoop
  - Post-tussive vomiting , Intracranial haemorrhage.

3. Convalescent: The coughing gradually subsides. Relapse can occur if another respiratory infection is acquired. This stage can last from 2 weeks to several months.

Pertussis in infants, adults and partially immunized individuals may not present with its typical clinical signs and symptoms.

Complications

The most common complication, and the cause of most pertussis-related deaths, is secondary bacterial pneumonia. Young infants are at highest risk for acquiring pertussis-associated complications. Pneumonia occurred in 5.2% of all reported pertussis cases, and among 11.8% of infants younger than 6 months of age. Neurologic complications such as seizures and encephalopathy (a diffuse disorder of the brain) may occur as a result of hypoxia (reduction of oxygen supply) from coughing, or possibly from toxin. Neurologic complications of pertussis are more common among infants. Other less serious complications of pertussis include otitis media, anorexia, and dehydration. Complications resulting from pressure effects of severe paroxysms include pneumothorax, epistaxis, subdural hematomas, hernias, and rectal prolapse.

Adolescents and adults may also develop complications of pertussis, such as difficulty sleeping, urinary incontinence, pneumonia, and rib fracture.

Complications in Children

- Secondary bacterial pneumonia – most common
- Neurologic complications – seizures, encephalopathy more common among infants
- Otitis media
- Anorexia
- Dehydration
- Pneumothorax
- Epistaxis
- Subdural hematomas
- Hernias
- Rectal prolapse

Complications in Adolescents and Adults

- Difficulty sleeping
- Urinary incontinence
- Pneumonia
- Rib fracture

8.9 Diagnosis

The diagnosis of pertussis is usually based upon a characteristic history and physical examination. However, laboratory tests may be useful in young infants, atypical cases and cases modified by vaccination.

The standard and preferred laboratory test for diagnosis of pertussis is isolation of B. pertussis by culture.

Fastidious growth requirements make B. pertussis difficult to isolate. Best results are obtained when cultures are done early during the catarrhal stage and before initiation of antibiotics. Serological testing is useful but is not yet standardized. Polymerase chain reaction (PCR) testing of nasopharyngeal swabs or aspirates has been found to be a rapid, sensitive and specific method for diagnosing pertussis.

8.10 Management

8.10.1 Antibiotic treatment

The medical management of pertussis cases is primarily supportive, although antibiotics are of some value to reduce infectivity. Macrolide antibiotics, such as erythromycin, may prevent or mitigate clinical pertussis when given during the incubation period or the early catarrhal stage. When given during the paroxysmal phase of the disease, antimicrobial drugs do not change the clinical course, but may eliminate bacteria from the nasopharynx and thus reduce transmission. Antimicrobial therapy should be continued for the full 14 days to minimize any chance of treatment failure. Antimicrobial drugs Azithromycin, clarithromycin may also use.

8.10.2 Isolation

Suspected cases should avoid contact with young children and women in late pregnancy, especially the unimmunized, until at least five days of antibiotics are taken. Ideally, untreated cases should avoid contact with high-risk individuals for the full infectious period. Hospitalized patients should be placed under respiratory isolation, or at a minimum apply contact and respiratory droplet precautions (such as wearing a mask when around other patients).

8.11 Prevention

Active primary immunization against B. pertussis infection is recommended with 3-dose pertussis toxoid-containing pentavalent vaccine, recommended with the first dose administered as early as 6 weeks of age. Subsequent doses should be given with an interval of at least 4 weeks between doses. The third dose of the primary series should be completed by 6 months of age.

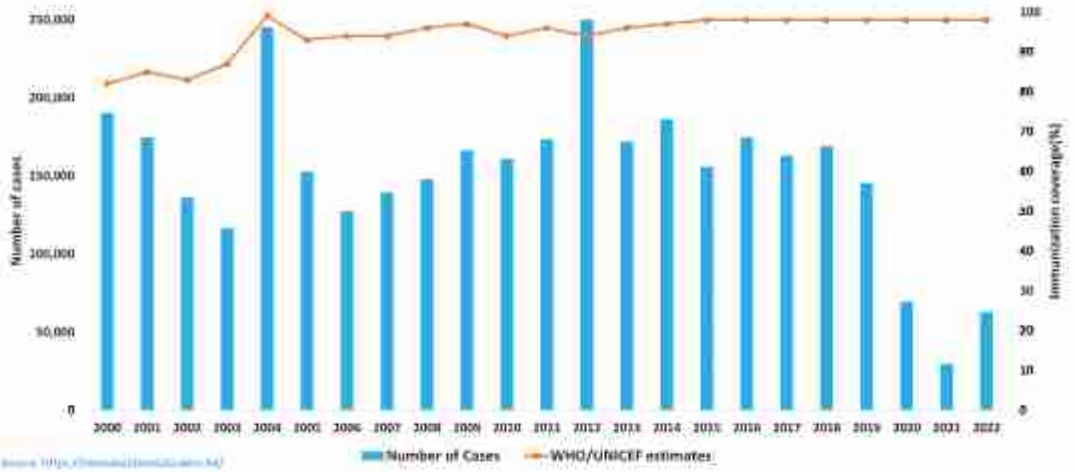
In general, pertussis vaccine is not given to persons 7 years of age or older, since reactions to the vaccine may be increased in older children and adults. In some cases of progressive neurologic illness the child should receive DT rather than pentavalent vaccine. In young infants with evolving and progressive neurologic disease, pertussis immunization may be delayed for some months to permit the diagnosis to be established and to avoid possible confusion about the cause of symptoms. The following are NOT contraindications to pertussis vaccination: stable neurologic disorders, such as well-controlled seizures; a family history of convulsive seizures; minor illness. Antipyretics may be given to the child if he/she should develop fever after vaccination to prevent febrile seizures.

8.12 Pertussis surveillance

Pertussis (whooping cough), caused by Bordetella pertussis, is endemic in all countries. Globally, it is estimated that there were 24.1 million pertussis cases and 160,700 deaths from pertussis in children < 5 years of age in 2014 , with periodic epidemics occurring every two to five years even after the introduction of effective vaccination programmes and the achievement of high vaccination coverage. Pertussis is transmitted from infected to susceptible individuals by airborne droplets[3]. In developing countries, although pertussis surveillance data is less robust, the average case-fatality ratio has been estimated at 4% in infants <12 months and 1% in children 1–4 years old; pertussis might account for 1% of mortality of children <5 years of age. Classical

pertussis is most often seen in pre-school and school aged children and Pertussis may be responsible for between 12% and 32% of chronic cough in adults.

Figure 30: Pertussis Global annual reported cases and DPT3 coverage 2000-2022



In Bangladesh, number of pertussis cases report through weekly passive surveillance during the period 2010-2022 declined remarkably as shown in table below.

Table 15: Pertussis reported cases, Bangladesh 2010-2022

Cases by Sex	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Male	6	20	6		6	6			1	3	1		
Female	11	22	7	1	6	5	1		2	9			
Unknown		2											
Grand Total	17	44	13	1	12	11	1	0	3	12	1	0	0

Age group	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	
0-11 Months		2	8		5	6			2	5			
1-4 years	5	13	1		1					1			
5-9 years	9	23	4	1	6	4	1		1	2			
10-14 years	2	4				1				4			
15+ years	1	2									1		
Pertussis Total	17	44	13	1	12	11	1	0	3	12	1	0	0

8.12.1 Case definition and final classification

Suspected Case

A person with a cough lasting at least 2 weeks with at least one of the following:

- paroxysms (i.e. fits) of coughing
- inspiratory whooping
- post-tussive vomiting (i.e. vomiting immediately after coughing)
- without other apparent causes

OR

Apnea (with or without cyanosis) in infants (age <1-year old) with cough of any duration

OR

If a physician suspects pertussis in a patient with cough of any duration.

Note: Pertussis in immunized or previously infected individuals can present without the classic signs of pertussis, and therefore might not be captured by the above case definition.

Description of case definition

Paroxysms of cough: cough becomes more frequent and spasmodic with repetitive bursts of 5–10 coughs, often within a single expiration. During a paroxysm, there may be a visible neck vein distension, bulging eyes, tongue protrusion and cyanosis. Frequency of paroxysmal episodes varies from several per hour to 5–10 per day. Episodes are often worse at night and interfere with sleep.

Whoop: Sound produced due to rapid inspiration against closed glottis at the end of cough paroxysm

Post-tussive vomiting: vomiting immediately after coughing occasionally with a mucous plug expelled at the end of an episode.

Without other apparent causes: exclude other causes of chronic cough, such as tuberculosis, asthmatic episodes, chronic bronchitis, etc.

8.12.2 Final case classification

Confirmed case

A confirmed case of pertussis may be determined by laboratory confirmation or epidemiological linkage.

- Laboratory confirmation: A laboratory-confirmed case is a person who meets the suspected case definition with laboratory confirmation by one of the following:
  - isolation of B. pertussis OR
  - detection of genomic sequences of B. pertussis by means of polymerase chain reaction (PCR) assay, if polymerase chain reaction (PCR) meets performance criteria outlined below OR
  - elevated IgG antibodies to pertussis toxin in an individual ≥11 years of age, one year or longer after last vaccine dose.

Culture and PCR detection of acute pertussis infection have higher specificity and are preferred diagnostic methodologies over serology. Serology should be reserved for cases ≥4 weeks from cough onset; however, IgG can sometimes remain elevated for more than a year after infection or vaccination, leading to potential false positives.

Epidemiologically linked case

An epidemiologically linked case is a person meeting the suspected case definition with close contact to a laboratory-confirmed case (or another epidemiologically linked case in an outbreak setting) in the three weeks prior to onset of cough. h Close contact is defined as having face-to-face exposure to a case, which includes household or family contact, people having stayed overnight in the same room with a case, and people having direct contact with respiratory, oral or nasal secretions with a laboratory-confirmed case.

Close contact is defined as having face-to-face exposure to a case, which includes household or family contact, people having stayed overnight in the same room with a case, and people having direct contact with respiratory, oral or nasal secretions with a laboratory-confirmed case.

Possible case

A person who meets the suspected case definition but does not meet confirmed classification as defined above should be considered a possible case. This includes suspected cases who did not have laboratory testing done and those who tested negative.

Discarded case

A patient that does not meet the clinical case definition on case investigation.

8.12.3 Rational and objectives of surveillance

- Monitor disease burden and the impact of the pertussis vaccination programme, with a special focus on understanding the morbidity and mortality in children < 5 years of age
- Generate data for strategic decisions to optimize the impact of vaccination
- Detect and guide public health response to outbreaks of pertussis.

8.12.4 Case notification

Reporting of all respiratory pertussis case should be done by attending doctors of the hospital/clinic through AFP and EPI disease report form. The filled-up report form should be submitted to Hospital Surveillance Officer on the same day. HSO should include the data of the case in the weekly line listing form and send it to the DSFP.

Cases of pertussis do not need to be reported immediately, but it should be reported to health authorities weekly. Identification of clusters of pertussis cases during the same time period and from the same geographic area would suggest a pertussis outbreak that would require investigation and response. Hence timely reporting of individual cases of pertussis is important. In addition, for better understanding of pertussis epidemiology it is necessary to determine geographic and demographic risk factors and case fatality of pertussis in Bangladesh and to develop immunization strategies for more effective prevention of pertussis morbidity and mortality.

8.12.5 Prevention of Spread

When cases of pertussis are identified, they should be kept in isolation for 5 days after they begin antibiotic treatment or for 21 days if they do not receive antibiotics. Articles soiled by nasal or throat discharges should be disinfected. All households and other close contacts should be provided prophylaxis with antibiotics. Contacts under 7 years old that have not received 3 doses of DPT should not interact with other children for at least 5 days after beginning antibiotic prophylaxis or for 21 days after the last exposure to the case if they do not receive antibiotic prophylaxis.

References:

1. *Epidemiology and prevention of vaccine preventable diseases-pertussis, CDC, USA*
2. *Surveillance guideline for VPDs -module 5, SEARO, WHO*
3. *Vaccine-Preventable Diseases Surveillance Standards-Pertussis, WHO*

9. Tuberculosis

9.1 Introduction

Tuberculosis (TB) is a contagious disease. Like common cold, it spreads through air. Only people who are infected with TB in their lungs (open case) are infectious. When infectious people cough, sneeze, talk or spit, they propel TB germs, known as bacilli into the air. A person needs only to inhale a small number of bacilli to be infected. Left untreated, each person with active TB will infect on an average between 10 and 15 people every year. But people infected with TB bacilli will not necessarily become sick with the disease. The immune system "walls off" the TB bacilli which protected by a thick waxy coat, can lie dormant for years. When someone's immune system is weakened, the chances of becoming sick are greater.

Childhood Tuberculosis

- Contagious Disease
- Causative agent: Usually Mycobacterium tuberculosis
- Usually attacks lungs
- Reservoir: Primarily humans, rarely primates
- Transmission: Through air from one person to another
- TB bacteria can attack any part of the body like kidney, spine. Brain

9.2 Causative agent

All species of the genus Mycobacterium share the property of acid-fastness. Four species in particular are referred to as the Mycobacterium tuberculosis complex because they share similar microbiological qualities and cause human disease: M. tuberculosis, M. africanum, M. ulcerans and M. bovis. In addition, M. avium intercellulare is a particularly common cause of disease among HIV-infected persons. Among all Mycobacteria, however, Mycobacterium tuberculosis is by far the most frequent and important cause of human disease.

9.3 Reservoir

Primarily humans, rarely primates; in some areas cattle, badgers, swine and other mammals are infected.

9.4 Communicability

Tuberculosis is communicable as long as viable tubercle bacilli are being discharged in the sputum. Some untreated or inadequately treated patients may remain intermittently sputum positive for years. The degree of communicability depends upon the number of bacilli discharged, the virulence of the bacilli, adequacy of ventilation, exposure of the bacilli to sun light or Ultra Violet (UV) light and opportunities of aerosolization by coughing, sneezing, talking or singing. Although effective antimicrobial therapy eliminates communicability within a few weeks, a full course of treatment is required for cure. Children with primary tuberculosis are generally not infectious.

9.5 Transmission

Exposure to tubercle bacilli in airborne droplet nuclei is produced by people with pulmonary or laryngeal tuberculosis during expiratory efforts like coughing, sneezing or singing. Direct invasion through mucous membranes or breaks in the skin may occur but is extremely rare. Bovine

tuberculosis results from exposure to tuberculous cattle, usually by ingestion of unpasteurized milk. Extrapulmonary tuberculosis is not communicable except in rare situations.

9.6 Susceptibility and resistance

The degree of susceptibility is directly related to the degree of exposure and does not appear to be related to genetic or other host factors. The most hazardous period for development of the disease is the first 6-12 months after infection. The risk of the disease is highest in children under 3 years, adolescents, very old and immuno-compromised persons such as those with HIV infection.

9.7 Prevention

The most important method to prevent tuberculosis is to prevent infection from known cases. This requires prompt identification, diagnosis and treatment of potential cases of tuberculosis before they spread the disease to others. Identification, diagnosis and treatment is facilitated by the availability of medical, laboratory and X-ray facilities for prompt examination of suspected cases and contacts. BCG immunization of uninfected people can induce tuberculin reactivity in more than 90% of the recipients. Although the effectiveness of BCG to prevent tuberculosis in adults is controversial, a large number of studies have consistently demonstrated protection against tuberculous meningitis and disseminated disease in children under 5 years of age. Finally, community education regarding the mode of spread, importance of early diagnosis, importance of completing treatment and methods of tuberculosis control is another component of tuberculosis prevention.

9.8 Clinical aspects of tuberculosis in children

Development of a demonstrable lesion or positive tuberculin reaction takes 2-10 weeks after infection with M. tuberculosis. In adults and older children with mature immune systems, 90% of infections result in lesions that heal and leave no residual changes other than pulmonary or tracheo-bronchial lymph node calcification (Ghon lesion). In children under 5 years old, however, clinical illness following infection is common and is classified as primary tuberculosis. Clinical illness may present as pulmonary tuberculosis or may spread hematogenously or through the lymphatic system to result in miliary, meningeal, or other forms of tuberculosis.

Clinical features of Tuberculosis in Children

- Cough
- Feelings of sickness or weakness, lethargy, and/or reduced playfulness;
- Weight loss or failure to thrive;
- Fever; and/or Night sweats

Most common TB in the lungs, but TB disease can affect other parts of the body. Symptoms of TB diseases depends on the area affected

Diagnosis of tuberculosis in children is difficult because the presenting symptoms are subtle. Children with pulmonary tuberculosis may be asymptomatic and pulmonary disease may be discovered coincidentally during a routine x-ray or examination as a contact of another case. Low grade fever, cough, listlessness and loss of weight may or may not be present. The tuberculin test is not always positive in infected children, especially if they are malnourished. Segmental collapse or lobar consolidation may develop shortly after initial infection in younger children; pleural effusions are

more common in older children. Children with miliary tuberculosis also present with low grade fever and wasting; cough, lymphadenopathy and/or splenomegaly may be present. The clinical presentation is similar to that of typhoid fever or malaria. Tuberculin test may be negative in some cases. Tuberculous meningitis is similarly insidious. Initial symptoms are non-specific and include intermittent fever, headache, anorexia, apathy and mild mental status changes. Vomiting may occur and meningeal signs eventually develop. Hydrocephalus may also occur due to raised intracranial pressure. Unlike bacterial meningitis, in which meningeal signs develop rapidly, the evolution of tuberculous meningitis usually takes 1-2 weeks. If left untreated, hemiparesis, convulsions and permanent cerebral damage develop. Among successfully treated cases, 25% remain with residual neurological deficits. Lumbar puncture usually reveals raised CSF pressure, clear or slightly turbid fluid, lymphocytosis (although neutrophils may predominate early in the disease), high protein and low sugar levels. Only 20% of CSF smears typically yield AFB in patients with tuberculous meningitis, although repeated lumbar puncture may increase the yield. Hence, a negative AFB smear from a lumbar puncture does not rule out tuberculous meningitis. Cultures are positive up to 80% of the time.

9.9 Treatment

Treatment regimes are different for children than for adults. Ethambutol is not recommended for children under the age of 6 years. Streptomycin is not recommended for pregnant women. The National Tuberculosis Control Programme adopted Directly Observed Treatment Short-course (DOTS) strategy for treatment.

9.10 Vaccines

BCG, or bacille Calmette-Guerin, is a vaccine to prevent TB disease. BCG is used in many countries to prevent childhood TB disease.

9.11 Childhood Tuberculosis Surveillance

The World Health Organization estimates that the largest number of new TB cases in 2016 occurred in the South-East Asia Region, which accounted for 36% of cases globally. The numbers of new cases are still increasing globally, each year, in the WHO regions of Africa, the Eastern Mediterranean and South-East Asia.

Tuberculosis (TB) is a major public health problem in Bangladesh since long. Under the Mycobacterial Disease Control (MBDC) unit of Directorate-General of Health Services (DGHS), National Tuberculosis Control Programme (NTP) is working with a mission of eliminating TB from Bangladesh. The goal is to reduce morbidity, mortality and transmission of TB until it will no longer be a public health problem.

9.11.1 Global Status

According to the 2016 WHO Global Tuberculosis Report, estimated new cases of tuberculosis (TB) were 10.4 million, of which about 1.0 million were children (<15 years of age), 5.9 million male and 3.5 million were female. It is estimated that with accurate diagnosis and good reporting systems, children less than 15 years are likely to contribute 4-22% of the disease burden in 22 high-burden countries of the world. With excellent TB control and active provision of preventive

therapy to child contacts, the burden of childhood TB can be reduced below 5%, as is the case in many developed countries. Because children acquire TB from the infectious adult cases, the incidence of pediatric TB provides an accurate measure of ongoing transmission within communities, a key indicator of epidemic control.

A common misperception used to be that children are not severely affected and that they rarely develop severe forms of disease. However, this is not the case in TB endemic areas where children often present with advanced disease and TB is a major contributor to under-5 morbidity and mortality. Global Tuberculosis Report 2015 estimates about 140,000 deaths from TB in children in 2014.

9.11.2 Bangladesh Status

In 2015, among all forms of 199,001 total TB cases 7984 were child TB (4.01%), which was 3.35% (6,262/186,968) in 2014, 2.78% (5,044/181,395) in 2013 and 3% (4,833/161,697) in 2012.

A study from 2008-09 in Madhupur upazilla in Tangail district showed an incidence of childhood TB of 52 per 100,000 among 0-14 year after a survey of all eligible children. Although this does not represent the national incidence of child TB, this figure indicates that there is a gap between the NTP-reported child TB and actual disease burden in the community. The NTP in 2007 and an NGO working with TB in 2009 reported detection rates of 9 and 8.6 per 100,000 0-14-year-olds, respectively.

A total of 223,921 cases or 221 per 100,000 populations reported to NTP in 2016. The lowest age group of reported cases to NTP is 0-14 years and breakdown of age group matching with EPI programme is not available. However, through weekly passive surveillance number of TB cases among under 5 years children reported are shown in table below:

Table 16: TB cases among children <5 years old, by Age Bangladesh 2010 – 2022

Cases by Age	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
0-11 MONTHS	4	7	3	11	5	5	5	2	0	2			
1-4 years	16	22	17	21	13	13	7	3	3	1			
TB Total	20	29	20	32	18	18	12	5	3	3			

(Source: BAN IVD database)

Only 5 tuberculosis cases among children <5 years old were reported to EPI in -2017, 3 case each in 2018, 2019 and '0' cases reported in last three years through the Weekly Passive Hospital Surveillance for EPI diseases which is under-reporting. Although childhood tuberculosis is clearly under-reported, most of the reported cases did not indicate the type of tuberculosis.

9.11.3 End TB Strategy

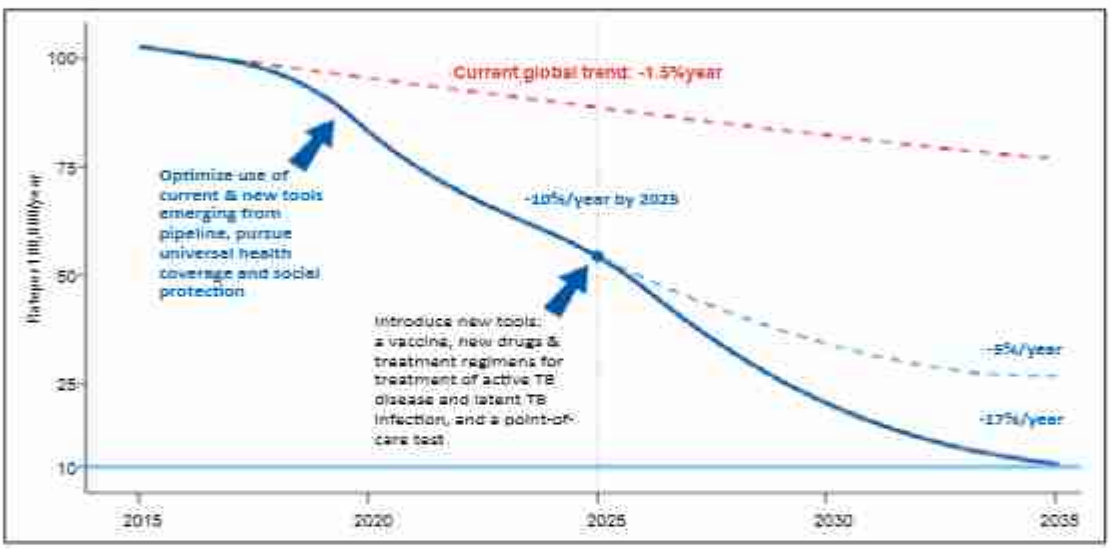
To reach the targets set out in the End TB Strategy, the annual decline in global TB incidence rates must first accelerate from 2% per year in 2015 to 10% per year by 2025. Secondly, the proportion of people with TB who die from the disease (the case-fatality ratio) needs to decline from a projected 15% in 2015 to 6.5% by 2025. These declines in deaths and incidence by 2025 while

ambitious are feasible with existing tools complemented by universal health coverage and social protection.

To sustain progress beyond 2025 and achieve the SDG* 2030 and End TB 2035 targets, additional tools must be available by 2025. In particular, a new vaccine that is effective pre- and post-exposure and a safer and more effective treatment for latent TB infection are needed to reduce the number of new TB cases arising from the approximately 2 billion people worldwide who are infected with M. tuberculosis, as well as better diagnostics and safer and easier treatment including shorter drug regimens for TB disease. For new tools to be available by 2025, greatly enhanced and immediate investments in research and development are required.

The figure below shows the projected acceleration of the decline in global TB incidence rates with optimization of current tools combined with progress towards universal health coverage and social protection from 2015, and the additional impact of new tools by 2025.

Figure 31: Projected acceleration of the decline in global TB incidence rates



9.11.4 Tuberculosis surveillance among children <5 years old in Bangladesh

Surveillance for tuberculosis in Bangladesh is done by the Mycobacterial Disease Control unit of Directorate-General of Health Services, Bangladesh. The purpose of the surveillance is primarily to identify, treat and track cases and to monitor for multi-drug resistant (MDR) tuberculosis. Although Upazila level tuberculosis registers list the age of each case, quarterly report forms indicate age groups only, the youngest being 0-14 years. Moreover, disease is classified as either pulmonary or extra pulmonary. Neither tuberculous meningitis nor miliary tuberculosis specifically can be reported. Hence, it is not possible to monitor or evaluate EPI program objectives of prevention of primary tuberculosis in children under 5 years age after BCG vaccination of infants through the Mycobacterial Disease Control (MBDC) unit. It is therefore important to include tuberculosis among children <5 years old as part of AFP & VPD Surveillance.

9.11.5 Surveillance case definition for tuberculosis (TB) in children <5 years old

A **probable case** of TB in a child will be defined as a child with:

- close contact with a case of tuberculosis, and
- an illness lasting >4 weeks, and
- unexplained fever, night sweats and failure to thrive (or weight loss), and
- for pulmonary tuberculosis: radiographic abnormalities consistent with pulmonary TB
- for tuberculous pleurisy: chest pain and radiographic findings showing a unilateral pleural effusion
- for tuberculous lymphadenitis: one or more large lymph nodes
- for tuberculous meningitis: mental status changes, headache and abnormal cerebrospinal fluid laboratory results
- for spinal tuberculosis: angle deformity of the spine
- for tuberculosis of the bone or joint: joint or bone swelling and pain
- for tuberculous peritonitis: signs of peritonitis and a palpable abdominal mass
- and/or ascites
- for miliary tuberculosis: characteristic "millet seed" appearance on chest radiograph or tuberculosis in more than one site as determined by a physician.

A **confirmed case** of TB in a child will be defined as any probable case with a Acid Fast Bacillus identified from clinical specimens or any child in which *Mycobacterium tuberculosis* is isolated from cultures of clinical specimens

Cases of tuberculosis in anyone should be reported *immediately* to public health authorities so that necessary measures may be taken in accordance with the National Tuberculosis Control Programme of Mycobacterial Disease Control (MBDC) unit of Directorate-General of Health Services (DGHS), Bangladesh.

References:

1. *cdc.gov/tb/topic/populations/tbinchildren/default.htm#:~:text=TB%*
2. *WHO Roadmap for childhood tuberculosis*
3. *who.int/news-room/fact-sheets/detail/tuberculosis*
4. *Bangladesh vaccine preventable diseases surveillance database*

EXPANDED PROGRAMME ON IMMUNIZATION

AFP & EPI DISEASE REPORT FORM

(Please use dates according to the English system)

Name of case: _____ **Date of Birth** (dd/mm/yy): ____/____/_____

Circle choices within boxes

Gender: Male / Female **Age**: years /months /days : _____

Name of Mother/father/husband: _____ Contact No. (if any): _____

Address: House/GR No. _____ Mahalla/Village _____

Ward:_____ Union: _____ Upazila/Municipality/CC: _____ District: _____

EPI Disease: *Place tick (√) mark next to disease[1] identified:*

____ AFP (in child <15 years)
____ Polio (any age)
____ Neonatal Tetanus (in child <28 days old)
____ Tetanus after neonatal period
____ Measles (any age)
____ CRS (<1 year)
____ Diphtheria (any age)
____ Pertussis (any age)
____ TB* in child <5 years
____ Acute Encephalitis Syndrome (AES)
_____ (type of TB*)

* *Please mention type of TB (Pulmonary/ Miliary / TB Meningitis/ Lymphadenitis/ Bone TB/ etc.)*

Date of onset of symptoms (dd/mm/yy): _____

Date of Hospital Visit (dd/mm/yy): _____ Hospital name _____

Information on last vaccination

Name of Vaccine	Dose (circle last valid dose)	Date last valid dose Received (dd/mm/yy)
BCG	1	
Penta	1 / 2 / 3	
MR	1	
OPV	1 / 2 / 3 / 4	
IPV	1 / 2	
TT/Td in mother (for Neonatal Tetanus case)	1 / 2 / 3 / 4 / 5	

Was the case fully vaccinated against this disease?[2] (Yes/No) : _____

Was diagnosis confirmed by lab? (Yes/No): _____

If yes, give result: _____

Did the patient die? (Yes/No): _____

If yes, date case died: (dd/mm/yy): _____

1. For case definitions, see inside cover of this book

2. Definitions of fully vaccinated:

AFP: 3 valid routine doses of OPV. **TB:** 1 valid dose of BCG. **Diphtheria/Pertussis/Tetanus/Hepatitis B/Haemophilus Influenzae Type b:** 3 valid doses of Penta. **Measles:** 2 doses of MR vaccine (1st dose at completion 9 months or 38 weeks or 270 days but before first birthday, and 2nd dose at 15 months of age but at least a month prior to rash onset. **NT:** Protected at birth if the mother had at least 2 valid TT/Td doses at least 2 weeks before but not more than 3 years before birth; 3 valid doses not more than 5 years before birth, 4 valid doses not more than 10 years before birth, or 5 valid doses. **CRS:** Protected at birth if the mother had at least 1 valid dose of Rubella/ MR/ MMR at least 1 month before her first conception or at least 2 weeks before last LRMP. It is assumed that 1 valid dose of rubella maintain lifelong immunity.

Notes:

1. If you find any case of Acute Flaccid Paralysis (*poliomyelitis, GBS, transverse myelitis, traumatic neuritis, etc.)* in a child under 15 years of age or Neonatal Tetanus or Measles or CRS or AES case, please report immediately to your DSFP and/or LSO and also inform the SIMO of your area.
2. For any child with pneumonia, diarrhoea, otitis media or xerophthalmia/ keratitis, physician should determine if he/ she had measles in past month; if yes, report the case as a measles case and complete this form.

Name of the person reporting: _____ *Signature:* _____

Designation: _____ *Date:* _____

Please fill out the form every time you see a new case of AFP or EPI disease and submit it to your HSO at the end of the day!

Approved by WHO. Updated: January **2023**

Annexure-2

EXPANDED PROGRAMME ON IMMUNIZATION

AFP & EPI Disease Weekly Line Listing Form for Hospitals and Upazila Health Complexes

(Please use dates according to the English system)

Facility name _____ City Corporation/ Municipality/Upazila: _____ District: _____

Reporting Epidemiologic week no: _____ Date from (Sunday): _____ *(dd/mm/yy)* to (Saturday): _____ *(dd/mm/yy)*

Summary number of cases: AFP: ☐ NT: ☐ Tetanus after neonatal period: ☐ Measles: ☐ AES: ☐

Diphtheria: ☐ Pertussis: ☐ Tuberculosis*: ☐ CRS: ☐

If no cases, write "0" in respective boxes

List any case of the EPI diseases including AFP (**<15 years old**), **Polio (any age)**, Neonatal Tetanus (**≤28 days old**), **Tetanus after neonatal period, CRS, Measles (any age)**, Pertussis/ Whooping cough (any age), Diphtheria (any age), or Tuberculosis (**≤5 years of age; *specify the type of tuberculosis** i.e., Pulmonary TB, Miliary TB, TB Meningitis, TB Lymphadenities, Bone TB, etc.) identified either in outpatient or inpatient setting. **Provide below details:**

Sl. No	EPID No. (AFP/Measles/NT/ CRS)	Disease	Patient name	Sex (M/F)	Patient's detailed address at time of infection including house # name, village/road/mahalla, ward, union, upazila/municipality and district whichever applicable	Date of birth (dd/mm/yy) or Age (specify d,m or y)	Date of symptom onset (dd/mm/yy)	Date of symptom visit (dd/mm/yy)	Fully Vaccinated against this disease (Yes or No)	Date case died (dd/mm/yy) (if applicable)

Prepared by: _____ *Name* _____ *Designation* _____ *Signature* _____ *Date*

Submitted by: _____ *Name* _____ *Designation* _____ *Signature* _____ *Date*

Your weekly report, including "0" reporting, must reach Civil Surgeon's Office of your district or CHO's Office by the following Tuesday

Supported by WHO, Updated: January 2023

Annexure-3

EXPANDED PROGRAMME ON IMMUNIZATION

AFP & EPI Disease Weekly Compilation Form for Districts/City Corporations

(Please use dates according to the English system)

District/CC: _____ Reporting Epidemiologic week no: _____ Date from (Sunday): _____ *(dd/mm/yy)* to (Saturday): _____ *(dd/mm/yy)*

No. of Reporting sites: _____ No. reported: _____ No. reported in time: _____

Summary number of cases: AFP: ☐ NT: ☐ Tetanus after neonatal period: ☐ Measles: ☐ AES: ☐

Diphtheria: ☐ Pertussis: ☐ Tuberculosis*: ☐ CRS: ☐

If no cases, write "0" in respective boxes

List any case of the EPI diseases including AFP (**<15 years old**), **Polio (any age)**, Neonatal Tetanus (**≤28 days old**), **Tetanus after neonatal period, CRS, Measles (any age)**, Pertussis/ Whooping cough (any age), Diphtheria (any age), or Tuberculosis (**≤5 years of age; *specify the type of tuberculosis** i,e., Pulmonary TB, Miliary TB, TB Meningitis, TB Lymphadenities, Bone TB, etc.) identified by your reporting sites, **Provide below details:**

Sl. No	EPID No. (AFP/Measles/NT/ CRS)	Disease	Patient name	Sex (M/F)	Union/ Urban Ward/ Mohalla	Upazila/ Municipality	Date of birth (dd/mm/yy) or Age (specify d,m or y)	Date of symptom onset (dd/mm/yy)	Fully Vaccinated against this disease (Yes or No)	Date case died (dd/mm/yy) (if applicable)	Remarks

Prepared by: _____ *Name* _____ *Designation* _____ *Signature* _____ *Date*

Submitted by: _____ *Name* _____ *Designation* _____ *Signature* _____ *Date*

Your weekly report, including "0" reporting, must reach Surveillance Section, EPI Bhaban, Mohakhali, Dhaka, by the following Sunday

Supported by WHO, January 2023

Annexure-4

EXPANDED PROGRAMME ON IMMUNIZATION

AFP, NT, Measles, CRS, and AES Weekly Active Surveillance Form

(Please use dates according to the English system)

Name of LSO/SMO: _____ Place of posting: _____

Reporting Epidemiologic week no: _____ Date from (Sunday): _____ to (Saturday): _____

(dd/mm/yy) *(dd/mm/yy)*

Hospital/UHC/Facility Name	District/ City Corporation/ Upazila/ Municipality	Date of visit (dd/mm/yy)	# AFP case/s	# NT case/s	# Measles case/s	# CRS case/s	# AES case/s

Sl. No	Hospital Name	Registered diagnosis as per hospital record*	EPID No (AFP/Measles/NT/ CRS)	Patient name and Father's name	Date seen at Hospital	Patient's detailed address at time of infection including house #/ name, village/road/mahalla, ward, union, upazila/municipality and district whichever applicable	Sex (M/F)	Date of birth (dd/mm/yy) or age (specify d,m,y)	Date of onset of paralysis, rigidity or rash (dd/mm/yy)	Fully Vaccinated against this disease (Yes or No)	Date of case investigation (dd/mm/yy)	Final case status (AFP, Measles, NT, CRS)

_____ _____

Signature *Date*

* Registered diagnoses of AFP may include polio, Guillian Barre Syndrome (GBS), transverse myelitis, traumatic neuritis, encephalitis, hemiplegia, hemiparesis, quadriplegia, quadriparesis, neuropathy, polyneuropathy, post-infective polyneuropathy, and others.

Your weekly report, including "0" reporting, must reach Surveillance Unit, EPI HQ, EPI Bhaban, Mohakhali, Dhaka, by the following Tuesday

Supported by WHO. Updated: January 2021

EXPANDED PROGRAMME ON IMMUNIZATION

ACUTE FLACCID PARALYSIS (AFP) CASE INVESTIGATION FORM

(Please complete every item, and use dates according to the English system)

BACKGROUND INFORMATION

DATE FOCAL PERSON WAS NOTIFIED: ___/___/___ NAME OF PERSON ORIGINALLY NOTIFYING:_____

DATE OF INVESTIGATION: ___/___/___ Designation/Address:_____

PATIENT IDENTIFICATION **CASE ID NUMBER: BAN -** ____-____-____-____ (District code, UPZ/MUN/CC code, Year, Case #)

Case name: _____ Father's name: _____

DATE OF BIRTH: ___/___/___ Sex: M / F (circle as appropriate) Religion:_____

House and Street Address: _____ Village/Mahalla: _____ Union/Ward #: _____

Upazila/Muni/CC: _____ District: _____ Contact Number (if any): _____

CLINICAL INFORMATION

1. Is or was paralysis present? YES ____ NO ____
2. Is the paralysis flaccid (floppy)? YES ____ NO ____
3. Did paralysis occur suddenly? YES ____ NO ____
4. *DATE OF PARALYSIS ONSET:* ___/___/___
5. Was paralysis caused by injury? YES ____ NO ____
6. Was paralysis present at birth? YES ____ NO ____

(If the answer to no. 1,2 or 3 is NO, or the answer to no. 5 or 6 is YES, the suspected AFP case is NOT confirmed AFP: Do *not* complete the rest of this form, and specify diagnosis, if known: _____)

SIGNS/SYMPTOMS

1. Fever when paralysis began? YES ___ NO ___ UNKNOWN ___
2. Muscle pain when paralysis began? YES ___ NO ___ UNKNOWN ___

3. SITE OF PARALYSIS *(mark all that apply)*

Right Arm ___ Left Arm ___
Right Leg ___ Left Leg ___
Neck ___ Face ___
Other: _____

4. Is paralysis asymmetric (NOT equal) on each side of body? YES ___ NO ___ UNKNOWN ___
5. Did paralysis begin in the feet or hands and move upward over time? YES ___ NO ___ UNKNOWN ___
6. Is sensation present in the site of paralysis? YES ___ NO ___ UNKNOWN ___
7. Was the child seen at a health facility? YES ___ NO ___ UNKNOWN ___

If yes, which? _____ Date of Visit / Admission: ___/___/___ Medical Record #: _____

VACCINATION HISTORY

	Number of Doses by Card	Number of Doses by History
1. Number of OPV doses received through campaigns (e.g. NID, Mop-up, MNT)	N/A	_____
2. Number of OPV doses received through routine EPI (with DPT/Penta/Measles/MR)	_____ OR	_____
3. Date of last OPV dose (routine *or* campaign) before paralysis onset: ___/___/___		
4. Number of IPV doses received	_____ OR	_____
5. Date of last IPV dose (routine or campaign) before paralysis onset: ___/___/___		

6. Was OPV given after paralysis onset? YES ___ NO ___ UNKNOWN ___ (If YES, date OPV was given: ___/___/___)

TRAVEL HISTORY

1. Did child travel outside his/her village/ mahalla during the 30 days before or after paralysis began? YES ___ NO ___ Unknown ___

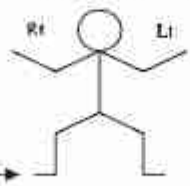
If YES, dates of travel: ___/___/___ to ___/___/___ Place of travel: House and Street Address if known: _____

Village/Mahalla: _____ Union/Ward: _____ Upazila/Muni/CC: _____ District: _____

If YES, notified to the concern DSFP/SIMO (for additional case/s and ORI)? YES ___ NO ___ **If YES**, date of notification: ___/___/___

CLINICAL EXAMINATION

Reflexes: (0-4+)



Planter Reflex
(Flexor/Extensor/Equivocal)

0 = No response
1+ = Somewhat diminished; low normal
2+ = Average; normal
3+ = Brisker than average; possibly but not necessarily indicative of disease
4+ = Very brisk; hyperactive

Strength: check following muscle groups for strength (put appropriate code number under Rt & Lt columns)

Codes: 0-5	STRENGTH	Rt	Lt	STRENGTH	Rt	Lt
0=No muscle contraction	Flex wrist			Flex hip		
1= Barely detectable contraction	Extend wrist			Extend hip		
2= Active movement, *not* against gravity	Flex elbow			Flex knee		
3 =Movement against gravity only	Extend elbow			Extend knee		
4= Movement vs. gravity+ mild resistance	Flex shoulder			Flex ankle		
5=Movement vs. full resistance (NORMAL)	Extend shoulder			Extend ankle		
	Hand Grip					

Supported by WHO. Updated January 2024

HISTORY OF PREVIOUS CONTACTS WITH HEALTH CARE PROVIDERS AFTER DATE OF PARALYSIS ONSET ***(start from most recent contact and proceed retrospectively)***

Name of Hospital/ Doctor/ Health care provider *(specify the category of the contact* in the table below)*	1.	2.	3.	4.
Address of Hospital/doctor/ Health Care provider				
Dates case visited				
Already in network?	Yes/ No/ Dk (circle)	Yes/ No/ Dk (circle)	Yes/ No/ Dk (circle)	Yes/ No/ Dk (circle)
Did they/ person report the case	Yes/ No (circle)	Yes/ No (circle)	Yes/ No (circle)	Yes/ No (circle)
Action taken/planned				

Category of the first health care provider (contact):** ***(Put tick mark in the box above appropriate category)

Regd doctor	GoB facility	Village doctor	NGO Clinic	Homeopath	Kabiraj	Imam	Pharmacist	HA	FWA	Other (specify):

Additional comments (Please use extra piece of paper if needed):

Suspected diagnosis: _____

ADDITIONAL INFORMATION

1. Was there any search for additional AFP cases? YES ___ NO ___ PENDING ___ If YES, additional AFP cases identified? YES ___ NO ___ If YES, how many? _____

2. Was outbreak response immunization done? YES ___ NO ___ PENDING ___ If YES, how many children were vaccinated? _____ If NO, explain _____

Note: If answer to question no. 1 & 2 is "Pending", complete the activities within 7 days of confirmation of AFP and share the updated form with EPI HQ

Case Investigated by: _____ Designation: _____ Signature: _____

Report sent by: _____ _____ _____ _____

Name Designation Signature Date

Send completed form with stool samples to the National Polio and Measles Laboratory (NPML), Institute of Public Health, Dhaka and ensure sample/s arrive within 72 hours of collection.

If there is no stool sample, send form to EPI HQ, Mohakhali, Dhaka; send copy to Civil Surgeon and SIMO. Keep one copy of this form for later review (e.g. during the 60+ Day Follow-up Exam).

STOOL SPECIMEN COLLECTION

	Date collected	Date Sent to NPML	*To be completed at NPML, IPH, Dhaka* Date Received at NPML
Specimen #1:	___/___/___	___/___/___	___/___/___
Specimen #2:	___/___/___	___/___/___	___/___/___

AFP cases to be investigated, and 2 stool samples to be collected as soon as possible. The 2ND stool sample to be collected 24 hours or more after collection of 1st sample.

Each stool sample must be sufficient in quantity *(at least 8 grams, or half an adult thumb, or half the container)*, sealed in separate containers, labeled with the AFP case name, case ID number, and collection date.

Samples to be maintained COLD in specimen carrier with 4 icepacks at <8°C Immediately after collection and until arrival at IPH, Dhaka. Icepacks to be changed every 24 hours.

FOR LABORATORY USE ONLY

CONDITION OF SPECIMENS

	Cold?	Moist?	Sufficient Quantity?	Leakage?	Result
Specimen 1:	YES___ NO___	YES___ NO___	YES___ NO___	YES___ NO___	_____
Specimen 2:	YES___ NO___	YES___ NO___	YES___ NO___	YES___ NO___	_____

_____ _____ _____ ___/___/___

Person delivering specimen Designation Signature Date

_____ _____ _____ ___/___/___

Person receiving specimen Designation Signature Date

Supported by WHO. Updated January 2024

EXPANDED PROGRAMME ON IMMUNIZATION

60+ DAY FOLLOW-UP EXAMINATION FORM

(Please complete every item, and use dates according to the English system)

PATIENT IDENTIFICATION **CASE ID NUMBER: AFP BAN -** _____-_____-_____-_____
(District code / UPZ/MUN/CC code / Year / Case #)

LAB ID: _____

Case name: _____ Father's name: _____

DATE OF BIRTH: ____/____/____ Sex: M / F Religion: _____ House and Street address: _____

If rural: Village: _____ Union: _____ Upazila: _____ District: _____

If urban: Mahalla: _____ Ward # : _____ Municipality or City Corp: _____District:_____

BACKGROUND INFORMATION

DATE OF PARALYSIS ONSET: ____/____/____ Date of original investigation: ____/____/____

FOLLOW-UP DATA

1. Was a 60+ Day Follow-Up Exam performed? YES ____ NO ____

If NO, 2. Why wasn't a 60+ Day follow-up examination done? (Circle one)
A. Patient died with date of death ____/____/____ B. Patient lost to follow-up C. Other: _____

If YES, *give the date of the 60+ Day Follow-Up Examination:* ____/____/____
dd mm yy

3. Is paralysis still present? YES ____ NO ____ ***If NO**, jump to number 9.*
4. Is the paralysis asymmetric? YES ____ NO ____
5. Is it flaccid (floppy)? YES ____ NO ____
6. Is there normal sensation? YES ____ NO ____

7. Assessment of muscle power: (Check following muscle groups for strength (put appropriate code number under Rt & Lt columns)

Codes: 0-5	STRENGTH	Rt	Lt	STRENGTH	Rt	Lt
0=No muscle contraction	Flex wrist			Flex hip		
1= Barely detectable contraction	Extend wrist			Extend hip		
2= Active movement, *not* against gravity	Flex elbow			Flex knee		
3 =Movement against gravity only	Extend elbow			Extend knee		
4= Movement vs. gravity+ mild resistance	Flex shoulder			Flex ankle		
5=Movement vs. full resistance (NORMAL)	Extend shoulder			Extend ankle		
	Hand Grip					

8. Site of muscle wasting at follow-up examination *(mark all that apply)*
Right Arm_____ Right Leg_____ Left Arm _____ Left Leg _____Other:_____ _____

9. If additional case finding and/or outbreak response immunization was "pending" at the time you submitted the AFP Case Investigation Form for Acute Flaccid Paralysis (AFP):

a. Was additional case finding done? YES ___ NO ___
If YES, were any additional AFP cases identified? YES ___ NO ___
If YES, how many? _____

b. Was outbreak response immunization done? YES ___ NO ___ If YES, how many children were vaccinated? _____

Additional comments:

Suspected diagnosis:

Clinical Investigator Name: _____ Designation: _____ Signature:_____

Reported by: _____ _____ _____ _____
Name *Designation* *Signature* *Date*

Supported by WHO. Updated: January 2024

Expanded Programme on Immunization
Epidemiological and Clinical Investigation of Potentially Compatible Polio Cases
(Additional Information on cases that may be referred to Expert Review Committee for Classification— information should be collected as early as possible after AFP case investigation if 2 adequate stools were not collected within 14 days of paralysis onset)

Investigator's name: _____ Designation: _____ Date of investigation____/____/___

Case I.D: EPID#_____ Lab # (if available)_____

Name of the case: _____ Age at onset: _____ Religion: _____

Address: Name of Father/(Guardian): _____ Village: _____

Union/Ward: _____ Upazila/Mun./CC: _____ District: _____

Initial Investigation / 60+ day follow-up findings (if applicable):

Date of onset: _____/_____/_____ Date of Initial Investigation: _____/_____/_____

Site of paralysis (circle): Right Arm/Left Arm Right Leg/Left Leg Other (specify)_____

Paralysis identified by (circle): Mother's history only/Physician's report/Investigation

Laboratory Results (circle): Stool 1- P1/P2/P3 Wild/Vaccine NPEV Negative Pending
Stool 2- P1/P2/P3 Wild/Vaccine NPEV Negative Pending

If potentially compatible case investigation is done 60 days or more after paralysis onset:
Residual weakness (at 60+ days): Yes/No/NA (circle) If NA, Died/Lost to Follow-up/ (circle)

Epidemiologic data: *(conduct as soon as possible)*
Area type: (circle) Rural/Peri-urban/ Urban Char/Haor/Hilly/Plain Land
Within 20 km of national border? Yes/No

Routine EPI status in ward:
Review EPI registration book for period 7-18 months ago No. newborns: _____ No. OPV3: _____

NID status in ward:
Review NID tally forms for ward from previous 2 years:

NIDs#____:	Dates: _____	Target: _____	Reached: _____
NIDs#____:	Dates: _____	Target: _____	Reached: _____
NIDs#____:	Dates: _____	Target: _____	Reached: _____
NIDs#____:	Dates: _____	Target: _____	Reached: _____

AFP Surveillance status in upazila/district
Case Clustering past 12 m in Upazila (consider municipality as part of sadar upazila):
No. of AFP cases _____ No. of compatible cases _____

- In neighboring upazilas?
  - _____ : No. of AFP cases _____ No. of compatible cases _____
  - _____ : No. of AFP cases _____ No. of compatible cases _____
  - _____ : No. of AFP cases _____ No. of compatible cases _____
  - _____ : No. of AFP cases _____ No. of compatible cases _____
  - _____ : No. of AFP cases _____ No. of compatible cases _____

Note: Attach map of the district showing all AFP cases in past 12 months indicating month of paralysis onset and which ones are compatible.

Expanded AFP Case Clinical Investigation

(Conduct as soon as possible)

Case name: _____ **EPID No.** _____

History of Present Illness

_____

_____

_____

_____

_____

_____

_____

_____

Difficulty swallowing? Yes/No Difficulty in urinating? Yes/No Difficulty in defecation? Yes/No

If yes, describe: _____

History of injection during week before paralysis onset? Yes/No

If yes, date and bodily location: _____

Past Medical History:

Has patient suffered from any of the following illnesses or disorders?

Illness	Yes	No	Illness	Yes	No	Illness	Yes	No	Illness	Yes	No
Arthritis			Cerebral Palsy			Headaches			Orthopedic problem		
Back problem			Epilepsy			Hearing loss			Rheumatic fever		
Birth defect			Fainting			Injury (serious)			Tinnitus (ringing ear)		
Cancer/tumor			Falls (serious)			Leukemia/lymphoma			Tuberculosis/Pott's		

IF ANY ANSWERED YES, OR OTHER SIGNIFICANT PMH, PLEASE GIVE DATES AND EXPLAIN

_____

_____

_____

Medications and dose before paralysis onset: _____

Allergies: _____

Physical Examination Findings:

Level of Consciousness (circle): Alert/Lethargic//Comatose-non responsive

Vital Signs: T: _____ P: ____ BP _____/_____ RR: _____ Weight: _____ Height: _____

Nutritional Status: Good/Fair/Poor/Very Poor

Skin: _____

HEENT:

Head (e.g., bruises, laceration, swelling): _____

Eyes: Conjunctiva: _____ Size of pupils (mm): R ___ L____ Reactive to light? Yes/No

Photophobia?: Yes/No

Ears: Hearing Intact? Yes/No

Neck: (circle one) supple or stiff

Lymph Nodes: (check if abnormal and describe)

Submandibular: ___: Cervical: ____ Supra/Subclavicular: ____ Axillary: _____ Inguinal: _____

Case name: _____ **EPID #:** _____

Spine: Scoliosis? Yes/No Mass? Yes/No Other deformity? Yes/No Bony tenderness: Yes/No
If any yes, describe: _____

Chest: Resonant? Yes/No Clear? Yes/No
Describe any abnormality: _____
Heart: Regular rhythm? Yes/No Murmur? Yes/No Other Abnormality: Yes/No
Describe any abnormality: _____
Abdomen: Soft: Yes/No Tender? Yes/No Masses? Yes/No Hepatomegaly? Yes/No
Splenomegaly: Yes/No
Describe any abnormality: _____

Musculo-skeletal: Any joint deformities? Yes/No Joint tenderness? Yes/No
Describe any abnormality: _____

Range of Motion-ROM (F=Full; P=Part; N=None) **Circumference** (In mm)

ROM	Rt	Lt	ROM	Rt	Lt	Circumference	Rt	Lt
Hands			Hips			Arm at bicep		
Wrists			Knees			Forearm		
Elbows			Ankles			Mid-thigh		
Shoulders			Toes			Mid-calf		

Brudzinski's Sign: Yes/No (with patient supine, passive flexion of neck causes legs to rise; raising of One leg causes contra-lateral leg to rise)
Kernig's sign: Yes/No (with patient supine, flex thigh against hip at right angle; then try to extend Leg/calf – positive sign is when you can't extend leg)

Neurological:

Eyes: Tonic (constant) deviation? Yes/No Nystagmus? Yes/No
If yes, describe: _____

Cranial nerves (√ s if normal; "X" if abnormal, and describes):

I: __ Olfactory – Have patient smell something distinctive with each nostril
II: __ Optic – Pupils equal and equally reactive to light? Visual fields intact by confrontation?
III, IV, VI ____ Oculomotor, Trochlear, Abducens: Extra-ocular eye movements in 6 directions
V: ___ Trigeminal (V1, V2, V3): Clench teeth; sensation on upper, middle, lower face; corneal reflex
VII: ___ Facial: Raise eyebrows, shut eyes so you can't open; smile; puff out cheeks
VIII: ____ Acoustic: hearing;
IX, X: ____ Glossopharyngeal, Vagus: Hoarse or nasal voice; palate upward with "ah"; gag reflex
XI: ___ Spinal accessory: Trapezius m. atrophy; shrug shoulders, turn head against resistance
XII: ____ Hypoglossal: stick out tongue, move from side to side; also look for tongue fasciculation;

Describe any abnormalities: _____

Strength: check following muscle groups for strength

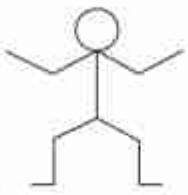
Codes: 0-5	STRENGTH	Rt	Lt	STRENGTH	Rt	Lt
0= No muscle contraction	Flex wrist			Flex hip		
1= Barely detectable contraction	Extend wrist			Extend hip		
2= Active movement, *not* against gravity	Flex elbow			Flex knee		
3= Movement against gravity only	Extend elbow			Extend knee		
4= Movement vs. gravity+ mild resistance	Flex shoulder			Flex ankle		
5= Movement vs. full resistance (NORMAL)	Extend shoulder			Extend ankle		
	Hand Grip					

Case name: _____ **EPID #:** _____

Sensation: Check pin-prick/soft touch on bilateral face, upper, mid, lower thorax/abdomen and back, upper arm, foream, hand, upper and lower leg, foot;
Check position sense on bilateral fingers and toes

Is sensation normal? Yes/No
Describle any abnormalities: _____

Reflexes: (0-4+)



Planter Reflex ——→
(Flexor/Extensor/Equivocal)

0 = No response
1+ = somewhat diminished; low normal
2+ = Average; normal
3+ = Brisker than average; possibly but not necessarily Indicative of disease
4+ = Very brisk; hyperactive

Cerebellar.
Romberg: Positive/Neg Finger-Nose: OK/Poor Heel-knee-shin: OK/Poor RAM:OK/Poor
If abnormal, describe: _____
Development milestones (neck raising, grab objects-6m; pincer grasp, crawi-9m; stand-12m; talk 2-3 y) Appropriate for age? Nes/No
If No, describe: _____

Other: _____

Laboratory Tests (list whatever available and write date collected next to entry; attach documents):

Hematology: WBC: _____ Diff: _____ Hgb: _____ HCT: _____ Platelets: _____

Chemistry: Sodium _____ Potassium _____ Chloride _____ CO2 _____ GLC _____
BUN: _____ Creatinine: _____

Urine: Sugar _____ Routine Examination _____

Stool: _____

CSF: Biochemical _____ Microscopic _____

Serology: _____

Special tests (if done, give dates and results; attach photocopies of reports)
X-rays : _____

Ultrasound _____

CT/MRI: _____

EMG/NCV _____

Other: _____

Diagnosis: _____

Signature of the Investigator _____ **Date** _____ / _____ / _____

Send copy to WHO-EPI, CS and keep one copy for your file

EXPANDED PROGRAMME ON IMMUNIZATION

Laboratory Request Form for Contacts' Samples

ID NUMBER of RELEVENT AFP CASE: BAN ____ _____ ____ _____
Dist Code Upazilla/Urb Code Year Case No

Name of Upazila/Municipality/CC: _____
Name of District: _____

CONTACTS DETAILS:

Sl. No	Contact's Name	Date of Birth or Age	Sex (M/F)	Guardian's Name	Name of Village / Mohalla	Name of Union / Urban Ward	OPV Doses (by history/card)		Date of Last Dose of OPV	Stool Sample Collection Date	Date Sample Sent to NPL-IPH	Contact's ID No:
							Routine	SIAs				
1												BAN ---- ---- ---- ---- C-1
2												BAN ---- ---- ---- ---- C-2
3												BAN ---- ---- ---- ---- C-3
4												BAN ---- ---- ---- ---- C-4
5												BAN ---- ---- ---- ---- C-5

Sample Sent By:

Name: ---------- **Designation:** ---------- **Signature:** ---------- **Date:** ----------

FOR LABORATORY USE ONLY

CONDITION OF SPECIMENS:

	Cold?	Moist?	Sufficient Quantity?	Leakage?
Specimen 1:	YES ___ NO___	YES ___ NO___	YES ___ NO___	___ NO___
Specimen 2:	YES ___ NO___	YES ___ NO___	YES ___ NO___	___ NO___
Specimen 3:	YES ___ NO___	YES ___ NO___	YES ___ NO___	___ NO___
Specimen 4:	YES ___ NO___	YES ___ NO___	YES ___ NO___	___ NO___
Specimen 5:	YES ___ NO___	YES ___ NO___	YES ___ NO___	___ NO___

Date of Stoool Specimen received at Lab: ___/___/_____

LABORATORY RESULTS

Enter 1=Yes, Wild; 2=Yes, Vaccine; 3=Yes, Pending IT Diff.; 4=Not Isolated; 5=No Specimen Processed

	P1	P2	P3
Specimen 1:	___	___	___
Specimen 2:	___	___	___
Specimen 3:	___	___	___
Specimen 4:	___	___	___
Specimen 5:	___	___	___

Enter 1=Yes; 2=No; 3=No Specimen
Non-Polio Enterovirus

___
___
___
___
___

Date when were results sent to EPI? ___/___/___
Lab Investigator: _____ **Date:** ___/___/___

Person Delivering Specimen	Designation	Signature	Date
			___/___/___

Person Receiving Specimen at Laboratory	Designation	Signature	Date
			___/___/___

EXPANDED PROGRAMME ON IMMUNIZATION

SUSPECTED MEASLES CASE INVESTIGATION FORM

(Please complete every item, and use dates according to the English System)

OUTBREAK ID: MSL BAN- _____ - _____ - _____ - _____
(District code - Upz/Mun/CC code - Onset Year - Outbreak #)

BACKGROUND INFORMATION **Is this INDEX CASE: Yes ____ No ____**

Date focal person was notified: ____/____/____ Name of person notifying: _____

Date of investigation: ____/____/____ Designation/Address: _____

Name of health facility: _____ Type of Health Facility: GOB ___ Non GOB___

Date of visit / admission: ____/____/____ Medical record #: _____

PATIENT IDENTIFICATION **CASE ID: MSL BAN-** _____ - _____ - _____ - _____
(District code - Upz/Mun/CC code - Onset Year - Case #)

Patient's Name: _____ Father's/Guardian's Name: _____ Contact Number: _____

Date of Birth: ____/____/____ OR Age: _____ Sex: ☐M ☐F House & Street Address: _____

If Rural: Village: _____ Union: _____ Upazila: _____ District: _____

If Urban: Mahalla: _____ Ward #: ____ Zone: ____ Municipality/CC: _____ District: _____

CLINICAL INFORMATION

1. Fever? ☐Yes ☐ No	**Date of onset of fever:** ___/___/_____
2. Generalized maculopapular rash? ☐Yes ☐ No	**Date of onset of rash:** ___/___/_____

ADDITIONAL CLINICAL INFORMATION

1. Cough? ☐Yes ☐No	2. Coryza? ☐Yes ☐No	3. Conjunctivitis? ☐Yes ☐No
4. Joint pain (arthralgia or arthritis)? ☐Yes ☐No 4a. If Yes, which joint/s (note all):		
5. Lymph node swelling (Lymphadenopathy)? ☐Yes ☐No 4a. If Yes, where (mark all that applicable):		
5a. Sub-occipital? ☐Yes ☐No	5b. Post auricular? ☐Yes ☐No	5c. Cervical? ☐Yes ☐No
6. Pregnant (when applicable)? ☐Yes ☐No ☐Unknown	6a. if yes, duration in weeks _____	

VACCINATION HISTORY

Type of Vaccine	Number of doses			Date of last dose (dd/mm/yyyy)
	Routine		SIA	
	By Card	By History		
MR				
Measles				
MMR				

TRAVEL HISTORY

Did the case travel outside his/her village/ mahalla during the 30 days before or within 7 days after rash onset OR any person visited the house/village/community of the case under investigation from an area/community of recent measles/rubella transmission during 30 days prior to rash onset?? YES ___ NO ___ Unknown ___. If YES, period of travel: ____/____/____ to ____/____/____
Place of travel: House and Street address (if known): _____ Village/Mahalla: _____
Union/Ward: _____ Upazila/Muni/CC: _____ District: _____

SPECIMEN COLLECTION

Specimen	Date collected	Date sent to NPML	To be completed at NPML, IPH, Dhaka	
			Date Received at NPML	Specimen Code
Serum (1st contact-28 days of rash onset)	___/___/___	___/___/___	___/___/___	
DBS ((1st contact-28 days of rash onset)	___/___/___	___/___/___	___/___/___	
Urine (within 5 days of rash onset)	___/___/___	___/___/___	___/___/___	
Nasopharyngeal swab (within 5 days of rash onset)	___/___/___	___/___/___	___/___/___	

(after collecting specimen(s), send this form and specimen(s) to HSO, Signature of MT-Lab_____ Date_____)

Case Investigated by: _____ Designation: _____ Signature: _____ Date: _____

Report sent by: _____ Designation: _____ Signature: _____ Date: _____

Supported by WHO. Updated: January 2023

FOR LABORATORY USE ONLY

SPECIMEN CONDITION

Specimen	Cold?	Sufficient Quantity?	Leakage?	Turbid?	Desiccated?
Serum	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No
DBS	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No
Urine	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No
Nasopharyngeal swab	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No

LABORATORY RESULT

Specimen	Test Result	Date of Result
Serum (IgM) for Measles	☐Positive ☐Negative ☐Equivocal ☐Pending ☐Not tested	__/__/__
Serum (IgM) for Rubella	☐Positive ☐Negative ☐Equivocal ☐Pending ☐Not tested	__/__/__
DBS (IgM) for Measles	☐Positive ☐Negative ☐Equivocal ☐Pending ☐Not tested	__/__/__
DBS (IgM) for Rubella	☐Positive ☐Negative ☐Equivocal ☐Pending ☐Not tested	__/__/__
Measles Virus Isolation		
Urine	☐Positive ☐Negative ☐Pending ☐Not tested	__/__/__
Nasopharyngeal swab	☐Positive ☐Negative ☐Pending ☐Not tested	__/__/__
Oral Fluid	☐Positive ☐Negative ☐Pending ☐Not tested	__/__/__
Genotype of Measles Virus:		__/__/__
Rubella Virus Isolation		
Urine	☐Positive ☐Negative ☐Pending ☐Not tested	__/__/__
Nasopharyngeal swab	☐Positive ☐Negative ☐Pending ☐Not tested	__/__/__
Oral Fluid	☐Positive ☐Negative ☐Pending ☐Not tested	__/__/__
Genotype of Rubella Virus:		__/__/__

Name of person delivering specimen: _____ Designation: _____ Signature: _____ Date: _____

Name of person receiving specimen: _____ Designation: _____ Signature: _____ Date: _____

FINAL CLASSIFICATION

☐ Clinically Compatible Measles ☐ Laboratory confirmed Measles ☐ Epidemiologically confirmed Measles

☐ Clinically Compatible Rubella ☐ Laboratory confirmed Rubella ☐ Epidemiologically confirmed Rubella

☐ Discarded

SOURCE OF INFECTION

☐ Endemic ☐ Imported ☐ Import related ☐ Unknown

ADDITIONAL COMMENTS (if any):

FOLLOW UP INFORMATION

1. Did the case Followed-up 30 days after rash onset? ☐ Yes ☐ No
2. Is or was there any complication as a result of Measles infection? ☐ Yes ☐ No
3. If Yes, what (mark all that apply)? ☐ ARI ☐ Diarrhoea ☐ Otitis media ☐ Malnutrition ☐ Encephalitis ☐ Others (Specify):_____
4. Outcome of the case: ☐ Alive ☐ Died

Measles: Form 1

Annexure-10

Outbreak Investigation: Measles Case Search

আউটব্রেক অনুসন্ধান: হামের রোগী অনুসন্ধান

Outbreak ID :

হামের আউটব্রেক আইডেন্টিফিকেশন নাম্বার:

গ্রাম: ওয়ার্ড: ইউনিয়ন/জোন:

উপজেলা/পৌরসভা: সিটি কর্পোরেশন: জেলা:

অনুসন্ধানের তারিখ: অনুসন্ধানকারী:

Row number	Age group	Number of Persons with measles vaccination (A)		Number of persons without measles vaccination (B)		Number of persons having measles disease(C)		Age specific Vaccination Coverage (%)
		Tally Mark	Number	Tally mark	Number	Tally mark	Number	
ক্রমিক নং	বয়স সীমা	হামের টিকা প্রাপ্ত ব্যক্তির সংখ্যা (এ)		হামের টিকা না পাওয়া ব্যক্তির সংখ্যা (বি)		হামের রোগীর সংখ্যা (সি)		বয়স ভিত্তিক টিকার অর্জন (%)
		ট্যালি	সংখ্যা	ট্যালি	সংখ্যা	ট্যালি	সংখ্যা	
১	< 9 Months < ৯ মাস							
২	9 Months - <1 Year ৯ মাস - < ১ বছর							
৩	1 - 4 Years ১ - ৪ বছর							
৪	5 - 9 Years ৫ - ৯ বছর							
৫	10 - 14 Years ১০ - ১৪ বছর							
৬	15- 19 Years ১৫ - ১৯ বছর							
৭	> = 20 Years >= ২০ বছর							

Notes:
লক্ষণীয়:

1. Details of all the persons (as per column C) who presently have measles or in the recent past had measles should be recorded in line list format (Form 2)
১. যাদের বর্তমানে হাম হয়েছে অথবা হালে আক্রান্ত ছিল (কলাম "সি" অনুযায়ী) তাদের বিস্তারিত তথ্য ফর্ম-২ তে লিপিবদ্ধ করুন।
2. Data on age breakup of population helps in calculation of Age specific attack rates and Vaccine Efficacy.
২. জনসংখ্যার বয়স বিন্যাস উপাত্ত বয়সভিত্তিক আক্রান্তের হার এবং ভ্যাকসিন এফিকেসি হিসাব করতে সহায়তা করবে।

Measles: Form 2

Annexure-11

Outbreak Investigation: Measles data analysis

District:

Upazila:

Union/ Ward: **Outbreak ID Number:**

Row No.	Age group	Total population in the age group (D)	Number of persons with measles vaccination (E)	Number of persons without measles vaccination (F)	Number of Measles cases (J)	Age specific attack rate %
1	< 1 year					
2	1 - 4 years					
3	5 - 9 years					
4	10 - 14 years					
5	15 - 19 years					
6	> = 20 years					
Total		0	0	0	0	

Notes: 1. Population in each age group is taken from Form 1. Add numbers in as per the instructions
2. Age specific attack rate is calculated as follows: for example, Age specific attack rate (5-9 years) per 100 population = J3 divided by D3 multiply by 100

EXPANDED PROGRAMME ON IMMUNIZATION

CONGENITAL RUBELLA SYNDROME (CRS) CASE INVESTIGATION FORM

(Please complete every item, and use dates according to the English system)

Lab No-

BACKGROUND INFORMATION

DATE FOCAL PERSON WAS NOTIFIED: ___/___/___ NAME OF PERSON ORIGINALLY NOTIFYING:_____

DATE OF INVESTIGATION: ___/___/___ Designation/Address:_____

Name of Health Facility..... Date of visit/admission..... Medical Record .....

PATIENT IDENTIFICATION **CASE ID NUMBER: BAN - _____-_____-____-____**
District code UPZ/MUN/CC code Year Case #

Case name: _____ Father's name: _____ Mother's Name:_____

DATE OF BIRTH: ____/____/____ Sex: M / F (circle as appropriate) Religion: _____

House and Street Address: _____

Village/Mahalla: _____Union: _____ Ward #: _____

Upazila/Muni/CC: _____ District: _____ Contact Number (if any): _____

CLINICAL INFORMATION (Tick as appropriate)

Group (a)

1. Congenital Heart Disease ☐Yes ☐No

If **'YES'** which of the followings (please **Tick** as appropriate): ☐PDA ☐VSD ☐CCHD ☐PS ☐Others (Specify)----------

2. Cataract ☐Yes ☐No 3. Congenital Glaucoma ☐Yes ☐No

4. Pigmentary retinopathy ☐Yes ☐No 5. Hearing impairment ☐Yes ☐No

Group (b)

1. Purpura ☐Yes ☐No 2. Spleenomegaly ☐Yes ☐No

3. Microcephaly ☐ Yes ☐No 4. Mental retardation ☐Yes ☐No

5. Meningoencephalitis ☐Yes ☐No 6. Radiolucent bone disease ☐Yes ☐No

7. Jaundice (within 24 hours after birth) ☐Yes ☐No

8. Other abnormalities ☐Yes ☐No (If yes, describe ----------)

Birth weight(lb) ---------- If died, date of death------/------/-----

---

MATERNAL HISTORY

Mother's age---------- No of previous pregnancies:----------

Vaccinated against rubella ☐Yes ☐No If **yes** date ----/----/----

Maculopapular rash illness with fever ☐Yes ☐No If **yes** write month during pregnancy------

If yes, was rubella laboratory confirmed ☐Yes ☐No

Exposed during pregnancy to any person with maculopapular rash illness with fever: Yes/No If **yes** write month-----

VACCINATION HISTORY OF THE CASE

Vaccinated against rubella: ☐Yes ☐No If **yes** date -----/-----/-----

LABORATORY TEST ON INFANT

Specimen	Date of collection	Date sent to NPML	Date Received at NPML, IPH, Dhaka
Blood (1ml)	_____/_____/_____	_____/_____/_____	_____/_____/_____

Rubella IgM test result Positive/Negative/Equivocal/Not tested Date of result : -----/----/-------

Other lab test results (if any) ---------- Date of result : -----/----/-------

Case Investigated by:_____ Designation: _____ Signature: _____ Date: _____

Report sent by: _____ Designation: _____ Signature: _____ Date: _____

Send completed forms with blood specimens to the National Polio& Measles Laboratory, Institute of Public Health, Dhaka so that they arrive within 48 hours after the time of specimen collection. If there is no blood specimen, send form to EPI HQ, Mohakhali, Dhaka; send copy to the civil surgeon and to the SMO.

FOR LABORATORY USE ONLY

SPECIMEN CONDITION (Please **Tick** as appropriate)

Specimen	Cold?	Sufficient Quantity?	Leakage?	Turbid?	Desiccated?
Serum	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No

Name of person delivering specimen: _____ Designation: _____ Signature: _____ Date: _____

Name of person receiving specimen: _____ Designation: _____ Signature: _____ Date: _____

CRS cases should be investigated, and 1 blood specimens should be collected as soon as possible. Specimen must be sufficient in quantity (at least 1 ml) must be sealed in separate specimen containers, labeled with the CRS case name, case ID number, and date of collection, and maintained COLD in a specimen carrier with ice packs at <8°C beginning immediately after collection and until arrival at IPH, Dhaka. Ice packs should be changed every 24 hours.

FINAL CLASSIFICATION

☐ Clinically confirmed CRS

☐ Laboratory confirmed CRS

☐ Congenital rubella infection (CRI)

COMMENTS:

EXPANDED PROGRAMME ON IMMUNIZATION

NEONATAL TETANUS CASE INVESTIGATION FORM

(Please complete every item, and use dates according to the English system)

DATE FOCAL PERSON WAS NOTIFIED: ___/___/___ NAME OF PERSON NOTIFYING:_____
DATE OF INVESTIGATION: ___/___/___ Designation/Address: _____

I. PATIENT IDENTIFICATION **CASE ID NUMBER: NT BAN -** _____ - _____ - _____ - _____
District code - Upz/Mun/CC code - Onset Year- Case #

INDEX CASE? YES ____ NO ____

Case name: _____ Father's name: _____ Mother's name: _____

DATE OF BIRTH: ___/___/___ Sex: M ___ F ___ House and Street address: _____

If rural: Village: _____ Union: _____ Upazila :_____ District: _____

If urban: Mahalla: _____ Ward # : _____ Municipality or City Corp: _____ District: _____

II. CLINICAL INFORMATION

1. What was the baby's age when he/she became sick? _____ DAYS Date of tetanus onset: ___/___/___
2. Was the baby able to suck milk and cry during the first 2 days of life? YES ____ NO ____
3. Did the baby's entire body become stiff when sick? YES ____ NO ____
4. Was the baby able to suck milk while sick? YES ____ NO ____

If the answer to #1 is NOT between 3 and 28 days, OR if the answers to either #2 or #3 are "NO" , OR if the answer to #4 is YES, it is not necessary to complete the rest of this form; give suspected diagnosis: _____

5. Did the baby have convulsions after becoming stiff? YES ____ NO ____
6. Did the baby have fever when stiff? YES ____ NO ____
7. Did the baby die? YES ____ NO ____ IF YES, DATE OF DEATH: ___/___/___

III. INFANT CARE

1. Where was the baby born? Hospital/clinic: _____ Home _____ Other ___ (Where:
2. Who cut the umbilical cord? Doctor ____ Nurse _____ FWV ___ Dai ____ Relative/Friend ____ Other: _____ designation
3. What was used to cut the cord? Wood ___ Shaving blade ___ Sterile blade ___ Other (specify): _____
4. Was a delivery kit used to deliver the baby? YES ____ NO ____ UNKNOWN _____
5. Was the child seen at a health facility? YES ____ NO ____ UNKNOWN _____

If yes, which? _____ Date of Visit / Admission: ___/___/___ Medical Record #: _____

IV. MOTHER'S VACCINATION HISTORY

1. Was mother ever vaccinated against tetanus? YES ____ NO ____

If YES,	No. doses by history	No. doses by card	Actual total no. doses
2. No. of valid TT/Td doses received:	_____	_____	___
3. Date of last valid TT/Td dose:	___/___/___	___/___/___	

2. Number of visits for Antenatal Checkup during the pregnancy: ____ ____

V. CASE RESPONSE

1. Was a case response conducted? YES ____ NO _____

IF YES, 2a. Were any additional NT cases (alive or dead) in the past 12 months identified? YES ___ NO ____

2b. IF YES, How many? _____

3a. Was the mother given TT/Td vaccine after detection of NT in her baby? YES ___ NO ____

3b. IF NO, why not? _____

Fill up the worksheet on the back of the form, and then complete the following:

4. How many total women 15-49 years old were screened? _____
5. How many total women 15-49 years old were eligible for Td1 + Td2? _____
6. How many total women were vaccinated with Td? _____

Clinical Investigator Name: _____ Designation: _____ Phone: _____

Reported by: _____ _____ _____ _____
Name *Designation* *Signature* *Date*

Phone number: _____

Supported by WHO. Updated: January 2024

Date of CRI: ____ / ____ / ____

Please send copy of completed investigation form to SIMO and EPI HQ, Mohakhali, Dhaka

Worksheet for Neonatal Tetanus Case Response

Instructions:

1. Visit all the households of the concern sub-block to find all women aged between 15-49 years eligible for Td as per Td-5 doses schedule. Explain that a baby of one of their neighbors died/ became sick from neonatal tetanus, and that they should be vaccinated so that both they and their future babies will be protected against this disease.
2. **If some of those eligible women who were not vaccinated on the day of Case Response Immunization (CRI), encourage them to attend the next routine EPI session.** Be sure to tell any woman receiving her first Td dose that she must receive a second dose soon after a month to be protected against tetanus.
3. Ensure CRI at the sub-block of NT case within 7 days of notification, record as date of CRI on top box of the form and send the same to data unit. Continue CRI in remaining sub-blocks/urban mahalla to cover the entire ward (within a month of notification).

Household	Number of 15-49 year old women in household	Number of these women eligible for Td this day	Number of 15-49 year old women eligible for					Total number of women vaccinated with Td
			Td1	Td2	Td3	Td4	Td5	
INDEX								
TOTALS								

Answer to Question V.4 Answer to Question V.5 Answer to Question V.6

Number of valid Td doses received	Next eligible Td dose	When eligible
None	Td1	Immediately
Td1	Td2	1 month or more after Td1
Td2	Td3	6 months or more after Td2
Td3	Td4	1 year or more after Td3
Td4	Td5	1 year or more after Td4
Td5	None	Fully protected

EXPANDED PROGRAMME ON IMMUNIZATION
ACUTE ENCEPHALITIS SYNDROME (AES) CASE INVESTIGATION FORM

Case EPID Number: AES – BAN - _____ - _____ - _____ - _____
(Syndrome – Country – District Code – Upz/ Mun/ CC Code – Onset Year – Unit Serial No. for the onset year)

A: REPORTING INFORMATION:

DATE FOCAL PERSON NOTIFIED: ___/___/___ *(dd/mm/yy)*
NAME OF PERSON NOTIFYING: _____
DATE OF INVESTIGATION: ___/___/___ *(dd/mm/yy)*
Designation / Address: _____

B: HOSPITAL INFORMATION:

Hospital name: _____ Date of admission: ___/___/___ *(dd/mm/yy)* Medical record number: _____
Diagnosis on admission: _____ Other (please specify): (_____)

C: PATIENT INFORMATION:

Patient name: _____ Father/Guardian's Name: _____ Religion: _____
Date of birth: ___/___/___ (dd/mm/yy) Age: _____ Years _____ Months Sex: _____ Male _____ Female
Occupation: _____ Contact Mobile No.: _____ _____ Tribal _____ Non-tribal
House/ Street address: _____ Village/ Mahalla: _____ Union/ Zone (CC): _____
Ward: _____ Upazila/ CC/ Mun.: _____ District: _____

D: ACUTE ENCEPHALITIS SYNDROME CASE DEFINITION[1]

1. Acute onset of fever	☐ Yes	☐ No	**Date of 1st Symptom onset:** ___/___/___ *(dd/mm/yy)*
2. Altered mental status (coma, lethargy, confusion, agitation)	☐ Yes	☐ No	
3. New onset seizures (excluding simple febrile seizures[2])	☐ Yes	☐ No	

E: SIGNS AND SYMPTOMS:

(check all that apply)	**Mental Status:** *(Pick MOST appropriate one)*	**Neurologic Details (Motor):** *(Pick MOST appropriate one)*
☐ Fever	☐ Normal	☐ Normal
☐ Seizures	☐ Mild/ Confused or disoriented/ Agitated	☐ Mild/ Abnormal tone
☐ Headaches	☐ Moderate/ Lethargic/ Decreased response	☐ Moderate/ Abnormal gait/Movements
	☐ Severe/ Coma/ Unconscious	☐ Severe/ Paralysis/ Limb weakness

F: IMMUNIZATION HISTORY:

Has the patient ever received Japanese encephalitis (JE) vaccine? ☐ Yes ☐ No ☐ Unknown
If Yes, Number of doses received: _____ Date of last JE immunization: ___/___/___ *(dd/mm/yy)*

G: TRAVEL HISTORY:

Did the patient travel outside of his/her home district in the 2 weeks before symptom onset? ☐ Yes ☐ No ☐ Unknown
If Traveled outside his/her home district, where: District: _____ Division: _____ Country (If other than Bangladesh): _____

H: LABORATORY RESULTS *(at any time during the period of illness)*:

Laboratory Test	Performed *(mark all that apply)*		Result (If performed, enter results)	
CSF white blood cells	☐ Yes	☐ No		
CSF protein	☐ Yes	☐ No		
CSF glucose	☐ Yes	☐ No		
CSF Gram stain	☐ Yes	☐ No		
CSF culture	☐ Yes	☐ No		
Haemophilus influenzae b	☐ Yes	☐ No	☐ Negative	☐ Positive
Streptococcus pneumoniae	☐ Yes	☐ No	☐ Negative	☐ Positive
Neisseria meningitidis	☐ Yes	☐ No	☐ Negative	☐ Positive *(Serogroup- A/ B/ C/ X/ Y/ W-135; please circle one)*
E. coli K1	☐ Yes	☐ No	☐ Negative	☐ Positive
Group B Streptococcus	☐ Yes	☐ No	☐ Negative	☐ Positive
Malaria PBF	☐ Yes	☐ No	☐ Negative	☐ Positive
Other Investigations *(done if any)*:				

[1] **Case definition of AES:** Clinically, a case of Acute Encephalitis Syndrome (AES) is defined as **a person of any age, in any geographical region, at any time of year** with the **acute onset of fever and a change in mental status** (include symptoms such as confusion, disorientation, coma, or inability to talk) AND/ OR **new onset of seizures** (excluding simple febrile seizure).

[2] ***Child 6 months to <6 years old whose only finding is fever and single generalized seizure lasting <15 minutes with recovery of consciousness within 60 minutes.***

Supported by WHO. Updated: January 2024

I: SPECIMEN COLLECTION AND TRANSPORTATION to JE LAB, IEDCR:

Sample Collection and Handling *(To be filled at Reporting Facility)*				Sample Condition *(To be Filled at Lab.)*				
Specimen Type	**Collected *(Put tick mark)***		**Date Collected**	**Date sent to Lab**	**Date received at Lab**	**Lab Code**	**Cold? (Y/N)**	**Volume adequate?**	**Leakage? (Y/N)**
Cerebrospinal fluid (CSF)[1]:	☐ Yes	☐ No	__/___/__	__/___/__	__/___/__				
Serum[1]:	☐ Yes	☐ No	__/___/__	__/___/__	__/___/__				

J: OUTCOME AT HOSPITAL: ***(immediately following events like discharge/ death/ other events like DOR/ DORB/ Absconded etc.)***

Did the patient survive or die?	☐ Survived ☐ Died ☐ Other *(please specify)*: _____
Date of discharge or death?	_____/_____/_____ *(dd/mm/yy)*

Investigated by: _____ Designation: _____ Signature: _____ Date: _____

Report sent by: _____ Designation: _____ Signature: _____ Date: _____

K: LABORATORY RESULTS FOR JE CONFIRMATION:

JE IgM ELISA: CSF		☐ Yes	☐ No	☐ Negative	☐ JE positive	☐ Equivocal
JE/ DEN IgM ELISA: Serum	☐ Yes	☐ No	☐ Negative	☐ JE positive	☐ DEN positive	☐ Equivocal
Nipah IgM ELISA: Serum	☐ Yes	☐ No	☐ Negative	☐ JE positive	☐ DEN positive	☐ Equivocal

L: FOLLOW-UP 6 MONTHS AFTER ONSET OF ILLNESS ***(Laboratory Confirmed JE case only)*:**

GPS Location of Lab. Confirm JE case ***(residence)*:**

Latitude: _____ **Longitude:** _____ **Accuracy** *(~5 m)*:

Was the patient followed up 6 months after the onset of illness? ☐ **Yes** ☐ **No**

If NO, Why wasn't? ____ Patient died with **date of death**: ___/___/____ *(dd/mm/yy)* ____ Patient lost to follow-up

If YES, date of follow-up: _____/_____/_____ *(dd/mm/yy)*

Does s/he have any **disability or sequelae resulting from this illness?** ☐ **Yes** ☐ **No** ☐ **Unknown**

If YES, what type *(check all that apply)*: ☐ **Weakness/ paralysis** ☐ **Seizures** ☐ **Movement disorder**
☐ **Other disability/sequelae (specify):** _____

Followed-up by: _____ Designation: _____ Signature: _____ Date: _____

Report sent by: _____ Designation: _____ Signature: _____ Date: _____

M: Final Classification ***(Check one as appropriate)*:**

☐ **Laboratory-confirmed JE**

☐ **Probable JE**

☐ **AES –unknown**

☐ **AES – other agent** *(specify other agent)*: _____

- ☐ **Laboratory-confirmed Bacterial Meningitis** *(specify the Pathogen)*: _____
- ☐ **Probable Bacterial Meningitis**
- ☐ **Laboratory-confirmed Dengue**
- ☐ **Laboratory-confirmed Nipah**

[1] ***CSF (is the preferred sample) and/or Serum sample to be collected on admission.***

Supported by WHO. Updated: January 2024

DIPTHERIA CASE INVESTIGATION FORM

Case ID: DIP BAN - _____ - _____ - _____ - _____
District Code - Upz/Mun/CC Code - Onset Year - Case #

I.CASE IDENTIFICATION/ DEMOGRAPHIC DETAILS

Patient name:	Father's name: Mother's name:	Ethnicity: ☐ Bengali ☐ Tribal & national ☐ Non-National	Guardian's Mobile No:
Date of birth:	____ /____/____	If date of birth unavailable, please indicate age in month or years: Age: _____ Year/s: _____ Month/s: _____	
Occupation:	Sex: ☐ Male ☐ Female	If Female of Child Bearing Age, Pregnancy Status: ☐ Pregnant ☐ Non-Pregnant	
If Rural: Village: _____	Ward: ____ Union: _____	Upazila: _____	District: _____
If Unban: Mahalla: _____	Ward: ____ Zone: ____	Municipality/City Corporation: _____	
Date of examination: (dd/mm/yy)	___/_____/_____	School name, if applicable:	

II. VITALS:

Heart rate:	Respiratory Rate:	Temp:
BP:	O_2 saturation:	AVPU:

III. BACKGROUND INFORMATION:

1. Number of Diphtheria containing vaccine doses received (DPT/Pentavalent/Td)

☐ Zero ☐ 1 ☐ 2 ☐ 3 ☐ >= 3

2. Date of last vaccination (dd/mm/yy)
_____ /_____ /_____

3. Source of vaccination information:
☐ by card ☐ by history

1. Contact with known case of Diphtheria/similar illness within 10 days prior to illness: ☐ Yes ☐ No ☐ Unknown ***If yes,*** details _____

2. Travel within 14 days from onset of illness: ☐ Yes ☐ No
If yes, from ____ /____ / ____ to ____ /____ / ____ Area: _____

3. Number of persons living in the household? _____
4. Number of accompanying care givers treated with antibiotics? _____
5. Other people with similar illness in the family?
☐ Yes ☐ No ***If yes,*** details _____
6. Attended health care facility in last 10 days: ☐ Yes ☐ No
If Yes, date: Name & Location:

IV. CLINICAL DETAILS

Date onset of fever and sore throat (dd/mm/yy): _____ /_____ /_____

Symptoms:	**Signs:**	**Complications:**	**Comorbid conditions:**
☐ Fever	☐ Pseudomembrane	☐ Respiratory distress	☐ Malnutrition
☐ Sore throat	☐ Gross cervical lymphadenopathy	☐ Shock	☐ Measles
☐ Difficulty swallowing	☐ Chest indrawing	☐ Irregular heart rate	☐ Acute watery diarrhoea
☐ Difficulty breathing	☐ Fast breathing rate	☐ Peripheral neuritis/neuropathy	☐ HIV suspected
☐ Nasal regurgitation	☐ Stridor	☐ Kidney failure	☐ Tuberculosis suspected
☐ Bloody nasal discharge	☐ Central cyanosis	☐ Cutaneous necrotic lesions	☐ Jaundice
☐ Ear discharge	☐ Fast heart rate	☐ Other, specify _____	☐ Pregnancy
☐ Drooling of saliva	☐ Decreased capillary refill (>3 s)		☐ Other, specify _____
☐ Change in voice	☐ Weakness		
☐ Swollen neck	☐ Lethargy		
☐ Skin ulcers	☐ Restlessness		
☐ Other, specify _____	☐ Other, specify _____		

Name of hospital/facility:	**Date of Visit:** _____ /____/_____ **Date of Admission:** _____ /____/_____	**Hospital Record No.:** _____

V. TREATMENT INFORMATION:

Administered antibiotic therapy? ☐ Yes ☐ No				
Type	Oral	IV/IM	Start date	End date
Penicillin				
Erythromycin				
Azithromycin				
Steroids				
Other, specify				

1. DAT treatment given: ☐ No ☐ Yes ***If No,*** why DAT was not given: ☐ DAT not available ☐ Referred
2. Sensitivity test done: ☐ No ☐ Yes ***If Yes,*** test results: ☐ hypersensitive ☐ no reaction

If hypersensitive, Pre-treatment given: ☐ No ☐ Yes ***If yes,*** ☐ antihistamine ☐ steroid ☐ adrenaline ☐ other, specify_____

4. Manufacturer of DAT: _____ Batch/Lot No. of DAT _____
5. Date of DAT administration (dd/mm/yy) ____/_____/ _____, Mode of administration: ☐ IV ☐ IM
6. Dose administered (units): _____
7. Side effects of DAT? ☐ No ☐ Yes. ***If yes,*** ☐ anaphylaxis ☐ febrile reaction ☐ other, describe _____
8. DAT infusion continued? ☐ No ☐ Yes

VI. SPECIMEN COLLECTION

Specimen/s collected? ☐ Yes ☐ No	
Date specimen/s collected: (dd/mm/yy): ____/____/____	Date specimen/s sent to Lab: ____/____/____
Type of sample: ☐ throat swab ☐ nasal swab ☐ piece of membrane ☐ skin swab	
Use of transport media? ☐ Amies ☐ Amies with charcoal ☐ any other, specify _____	
Transported in cold chain (2°-8° C)? ☐ Yes ☐ No	
Lab results for C. Diphtheria	☐ Positive ☐ Undetermined
Date of results: ____/____/____	☐ Negative ☐ Not processed

VII. DISCHARGE DETAILS

Date of Discharge	____/____/____

Outcome at discharge

☐ Clinically well and discharged
☐ Death: date _____/_____/_____ Cause: _____
☐ Referred to _____ date: _____/_____/_____
☐ Left hospital against medical advice (e.g. DOR/DORB)
☐ Recovered with clinical sequela: ☐ palatal palsy ☐ neurologic deficit ☐ renal failure ☐ arrhythmia/heart failure ☐ Other, specify _____

Case Investigated by: _____ _____ _____ ___/___/___
Name *Designation* *Signature* *Date*

Report sent by: _____ _____ _____ ___/___/___
Name *Designation* *Signature* *Date*

VIII. 30 DAY FOLLOW-UP *(for Lab. confirmed and epi-linkend case only since the date of intital investigation)*

Date of follow-up: _____/_____/_____
☐ Full recovery
☐ Death: date of death _____/_____/_____ Cause of death: _____
☐ Recovery with clinical sequela: ☐ palatal palsy ☐ neurologic deficit ☐ renal failure
☐ arrhythmia/heart failure ☐ Other, specify _____

Case Followed-up by: _____ _____ _____ ___/___/___
Name *Designation* *Signature* *Date*

Report sent by: _____ _____ _____ ___/___/___
Name *Designation* *Signature* *Date*

LABORATORY REQUEST FORM (LRF): Suspected DIPTHERIA Case Specimen/s

Lab Code: _____

Case ID: DIP BAN - _____ - _____ - _____ - _____

District Code - Upz/Mun/CC Code - Onset Year - Case #

Specimen/s collected from: ☐ **index case** ☐ **suspected contact**

☐ **suspected case identified during contact tracing (no H/O contact)**

Patient/suspected contact Name: _____ **Sex:** M / F *(circle as appropriate)*

Date of Birth (dd/mm/yy): ____ / ____ / ____ **OR Age:** _____ Mon / Yr *(circle as appropriate)* **Religion:** _____

Father's/Guardian Name: _____ **Mother's Name:** _____

If Rural: Village: _____ Ward: ____ Union: _____ Upazila: _____ District: _____

If Unban: Mahalla: _____ Ward: ____ Zone: _____ Municipality/City Corporation: _____

Date of onset of fever and sore throat *(dd/mm/yy)*:

Date of sample collection *(dd/mm/yy)*:

Type of sample *(put tick as appropriate)*: ☐ throat swab ☐ nasal swab ☐ piece of membrane ☐ skin swab

Meida used to transport specimen/s: ☐ Not used ☐ Amies ☐ Stuart ☐ Amies with charcoal

☐ Any other *(specify)*: _____

Case selection criteria:

- ☐ Case with typical signs and symptoms with pseudo-membrane
- ☐ Contact/s with suspicion of diphtheria
- ☐ Suspected case *(with no H/O contact with Index case)*
- ☐ Atypical presentation with no pseudo-membrane but with bull neck or danger signs
- ☐ Cutaneous Diphtheria

Name of sender: _____

Phone number: _____ Email address: _____

Signature: _____ Date: _____

LABORATORY RECIEPT

Lab Code: _____

Case ID: DIP BAN - _____ - _____ - _____ - _____

District Code - Upz/Mun/CC Code - Onset Year - Case #

Date sample received (dd/mm/yy): ____ / ____ / ____

Condition of specimen received: ☐ Good ☐ Poor; **If poor**, please specify the reason (put tick as appropriate):

☐ cold chain not maintained ☐ sample leaked ☐ not in transport media ☐ Other _____

Name of receiver: _____

Phone number: _____ Email address: _____

Signature: _____ Date: _____

Contact Tracing for Prophylaxis & Daily Monitoring *(to be filled by Field Workers/Volunteers)*

Case ID: _____ Patient name: _____ Contact tracer's name: _____ Agency/Organization: _____

Village/ Mahalla: _____ Street No.: _____ Ward: _____ Union/Zone: _____ Uzila/Municipality/City Corporation: _____ GPS location of case: _____

									Day 1 visit date: ___/___/___ First dose of antibiotic		Day 2 visit date: ___/___/___ Second dose of antibiotic		Day 3 visit date: ___/___/___ Third dose of antibiotic		
	Name / Surname of contact (1 person per line)	Father/Guardian's Name	Age of the contact (in years)		Contact with fever/ sore throat (✓/ X)	Antibiotic dose (e.g. 250mg)	Contact unvaccinated (✓ if unvaccinated)		Taken under observation (✓/ X)	Taken without observation (✓/ X)	Taken under observation (✓/ X)	Taken without observation (✓/ X)	Taken under observation (✓/ X)	Taken without observation (✓/ X)	Comments (mention if contact died, migrated, etc.)
			Less than 7 years	7 years and above			Less than 7 years	7 years and above							
1															
2															
3															
4															
5															
6															
7															
8															
9															
10															
11															
12															
13															
14															
15															
Reporting totals:		Total of contacts traced: _____					Total of contacts unvaccinated: _____		Total DOT day 1: ___		Total DOT day 2: ___		Total DOT day 3: ___		

Comments:

Signature of supervisor: _____

! Oral Azithromycin should be given two hours after food and no food intake for another 1-2 hours after the medication.

Antibiotic: Oral Azithromycin 250 mg	Dose	Duration
< 1 year	1/2 tablet	3 days
1-5 years	1 tablet	3 days
>5 years	2 tablets	3 days

Line list of CONTACT children aged 6 weeks - 6 Years (6 year 11 months 29 days) for PENTA vaccination

Aria Information: Sub-block/Mohalla:

Ward: Union/Zone: Upazila: District: District:

S.N.	Name	Name of Father	Age (year)	Availability of Card	Date of Vaccination by EPI Card			Vaccination Eligibility (B=Booster or P=Primary series)	Vaccine provided			
				Y/N	DPT/Penta-1	DPT/Penta-2	DPT/Penta-3		Booster	Penta-1	Penta-2	Penta-3

Line list of CONTACT aged 7 Years and above for Td vaccination

Aria Information: Sub-block/Mohalla:

Ward: Union/Zone: Upazila: District: District:

S.N.	Name	Name of Father	Age (year)	Availability of Card	Date of Vaccination by EPI Card			Vaccination Eligibility (B=Booster or P=Primary series)	Date of Vaccination			
				Y/N	DPT/Penta-1	DPT/Penta-2	DPT/Penta-3		Booster	Td-1	Td-2	Td-3

Annexure-20

EXPANDED PROGRAMME ON IMMUNIZATION

Suspected /Confirmed AFP Line Listing Form

(Please use dates according to the English System)

Thana/Municipality/City Corporation:_____ District:_____ Year:_____

Thana/Municipality/City Corporation Code #:_____ District Code #:_____

Sl.#	Case ID #	Name	Detailed Address (include community or mahalla ward, and union)	Sex (M/F)	Date of Birth (dd/mm/yy)	Report site (H or C)*	Date Reported (dd/mm/yy)	Date of Paralysis (dd/mm/yy)	Date of Investigated (dd/mm/yy)	Confirmed AFP? (Yes or No)	Dates stool collected(dd/mm/yy)	Date and result of 60+day Follow Up	Stool Results (Pos or Neg)	Final Classification

H = Hospital Reported By : _____ _____ _____ _____

C = Community Name Designation Signature Date

(Keep this form available for review all times)

Code List for Districts- 2020
(Upazilas, Municipalities and City Corporations)

DIVISION	DIVISION CODE	DISTRICT	DISTRICT CODE	UPAZILA/ MUNICIPALITY/ CITY CORPORATION	UPAZILA/ MUNICIPALITY/ CITY CORPORATION CODE	TYPE OF AREA
BARISAL	04	BARGUNA	48	BARGUNA S	399	Upz
BARISAL	04	BARGUNA	48	AMTALI	400	Upz
BARISAL	04	BARGUNA	48	BAMNA	401	Upz
BARISAL	04	BARGUNA	48	BETAGI	402	Upz
BARISAL	04	BARGUNA	48	PATHARGHATA	403	Upz
BARISAL	04	BARGUNA	48	BARGUNA MUN.	404	Mun
BARISAL	04	BARGUNA	48	TALTOLY	550	Upz
BARISAL	04	BARISAL	43	BAKERGANJ	360	Upz
BARISAL	04	BARISAL	43	BARISAL S	361	Upz
BARISAL	04	BARISAL	43	BABUGANJ	362	Upz
BARISAL	04	BARISAL	43	WAZIRPUR	363	Upz
BARISAL	04	BARISAL	43	AGAILJHARA	364	Upz
BARISAL	04	BARISAL	43	GAURNADI	365	Upz
BARISAL	04	BARISAL	43	MULADI	366	Upz
BARISAL	04	BARISAL	43	HIZLA	367	Upz
BARISAL	04	BARISAL	43	MEHENDIGANJ	368	Upz
BARISAL	04	BARISAL	43	BARISAL CC.	369	CC
BARISAL	04	BARISAL	43	BANARIPARA	370	Upz
BARISAL	04	BARISAL	43	BAKERGANJ MUN.	590	Mun
BARISAL	04	BHOLA	45	BHOLA S	378	Upz
BARISAL	04	BHOLA	45	BURHANUDDIN	379	Upz
BARISAL	04	BHOLA	45	CHAR FASSON	380	Upz
BARISAL	04	BHOLA	45	DAULATKHAN	381	Upz
BARISAL	04	BHOLA	45	LALMOHAN	382	Upz
BARISAL	04	BHOLA	45	MANPURA	383	Upz
BARISAL	04	BHOLA	45	TAJUMUDDIN	384	Upz
BARISAL	04	BHOLA	45	BHOLA MUN.	385	Mun
BARISAL	04	BHOLA	45	LALMOHAN MUN.	555	Mun
BARISAL	04	BHOLA	45	CHAR FASSON MUN.	585	Mun
BARISAL	04	JHALAKATI	47	JHALAKATI S	393	Upz
BARISAL	04	JHALAKATI	47	KATHALIA	394	Upz
BARISAL	04	JHALAKATI	47	NALCHITY	395	Upz
BARISAL	04	JHALAKATI	47	RAJAPUR	396	Upz
BARISAL	04	JHALAKATI	47	JHALAKATI MUN.	397	Mun
BARISAL	04	JHALAKATI	47	NALCHITI MUN.	398	Mun
BARISAL	04	PATUAKHALI	44	KALAPARA	371	Upz
BARISAL	04	PATUAKHALI	44	MIRZAGANJ	372	Upz
BARISAL	04	PATUAKHALI	44	PATUAKHALI S	373	Upz
BARISAL	04	PATUAKHALI	44	BAUPHAL	374	Upz
BARISAL	04	PATUAKHALI	44	GALACHIPA	375	Upz
BARISAL	04	PATUAKHALI	44	DASMINA	376	Upz
BARISAL	04	PATUAKHALI	44	PATUAKHALI MUN.	377	Mun
BARISAL	04	PATUAKHALI	44	DUMKI	573	Upz
BARISAL	04	PATUAKHALI	44	RANGABALI	616	Upz
BARISAL	04	PEROJPUR	46	PIROJPUR S	386	Upz
BARISAL	04	PEROJPUR	46	BHANDARIA	387	Upz
BARISAL	04	PEROJPUR	46	KAUKHALI	388	Upz
BARISAL	04	PEROJPUR	46	MATHBARIA	389	Upz

DIVISION	DIVISION CODE	DISTRICT	DISTRICT CODE	UPAZILA/ MUNICIPALITY/ CITY CORPORATION	UPAZILA/ MUNICIPALITY/ CITY CORPORATION CODE	TYPE OF AREA
BARISAL	04	PEROJPUR	46	NAZIRPUR	390	Upz
BARISAL	04	PEROJPUR	46	NESARABAD/Swarupakati	391	Upz
BARISAL	04	PEROJPUR	46	PEROJPUR MUN.	392	Mun
BARISAL	04	PEROJPUR	46	MATHBARIA MUN.	556	Mun
BARISAL	04	PEROJPUR	46	ZIANAGAR/INDURKANI	574	Upz
CHITTAGONG	01	BANDARBAN	05	BANDARBAN S	044	Upz
CHITTAGONG	01	BANDARBAN	05	ROWANGCHHARI	045	Upz
CHITTAGONG	01	BANDARBAN	05	RUMA	046	Upz
CHITTAGONG	01	BANDARBAN	05	THANCHI	047	Upz
CHITTAGONG	01	BANDARBAN	05	LAMA	048	Upz
CHITTAGONG	01	BANDARBAN	05	ALI KADAM	049	Upz
CHITTAGONG	01	BANDARBAN	05	NAIKHONGCHARI	050	Upz
CHITTAGONG	01	BANDARBAN	05	BANDARBAN MUN.	051	Mun
CHITTAGONG	01	BRAHMANBARIA	07	AKHAURA	066	Upz
CHITTAGONG	01	BRAHMANBARIA	07	SARAIL	067	Upz
CHITTAGONG	01	BRAHMANBARIA	07	NABINAGAR	068	Upz
CHITTAGONG	01	BRAHMANBARIA	07	KASBA	069	Upz
CHITTAGONG	01	BRAHMANBARIA	07	BRAHMANBARIA MUN.	070	Mun
CHITTAGONG	01	BRAHMANBARIA	07	BRAHMANBARIA S	071	Upz
CHITTAGONG	01	BRAHMANBARIA	07	BANCHARAMPUR	072	Upz
CHITTAGONG	01	BRAHMANBARIA	07	NASIRNAGAR	073	Upz
CHITTAGONG	01	BRAHMANBARIA	07	ASHUGANJ	576	Upz
CHITTAGONG	01	BRAHMANBARIA	07	BIJOYNAGAR	581	Upz
CHITTAGONG	01	CHANDPUR	08	CHANDPUR S	074	Upz
CHITTAGONG	01	CHANDPUR	08	FARIDGANJ	075	Upz
CHITTAGONG	01	CHANDPUR	08	HAJIGANJ MUN.	076	Mun
CHITTAGONG	01	CHANDPUR	08	KACHUA	077	Upz
CHITTAGONG	01	CHANDPUR	08	MATLAB	078	Upz
CHITTAGONG	01	CHANDPUR	08	SHAHRASTI	079	Upz
CHITTAGONG	01	CHANDPUR	08	HAIMCHAR	080	Upz
CHITTAGONG	01	CHANDPUR	08	CHANDPUR MUN.	081	Mun
CHITTAGONG	01	CHANDPUR	08	HAJIGANJ	082	Upz
CHITTAGONG	01	CHANDPUR	08	MATLAB NORTH	566	Upz
CHITTAGONG	01	CHITTAGONG	01	BOALKHALI	001	Upz
CHITTAGONG	01	CHITTAGONG	01	MIRSHARAI	002	Upz
CHITTAGONG	01	CHITTAGONG	01	CHITTAGONG CC.	003	CC
CHITTAGONG	01	CHITTAGONG	01	RANGUNIA	004	Upz
CHITTAGONG	01	CHITTAGONG	01	RAOZAN	005	Upz
CHITTAGONG	01	CHITTAGONG	01	PATIYA-Karnafully	006	Upz
CHITTAGONG	01	CHITTAGONG	01	SITAKUNDA	007	Upz
CHITTAGONG	01	CHITTAGONG	01	SATKANIA	008	Upz
CHITTAGONG	01	CHITTAGONG	01	FATIKCHHARI	009	Upz
CHITTAGONG	01	CHITTAGONG	01	HATHAZARI	010	Upz
CHITTAGONG	01	CHITTAGONG	01	SANDWIP	011	Upz
CHITTAGONG	01	CHITTAGONG	01	ANWARA	012	Upz
CHITTAGONG	01	CHITTAGONG	01	BANSHKHALI	013	Upz
CHITTAGONG	01	CHITTAGONG	01	CHANDANAISH	014	Upz
CHITTAGONG	01	CHITTAGONG	01	LOHAGARA	015	Upz
CHITTAGONG	01	CHITTAGONG	01	KARNAPHULI	808	Upz
CHITTAGONG	01	COMILLA	06	MURADNAGAR	052	Upz
CHITTAGONG	01	COMILLA	06	CHOUDDAGRAM	053	Upz
CHITTAGONG	01	COMILLA	06	DEBIDWAR	054	Upz
CHITTAGONG	01	COMILLA	06	COMILLA CC.	055	CC

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CHITTAGONG	01	COMILLA	06	CHANDINA	056	Upz
CHITTAGONG	01	COMILLA	06	DAUDKANDI	057	Upz
CHITTAGONG	01	COMILLA	06	BARURA	058	Upz
CHITTAGONG	01	COMILLA	06	COMILLA S (Adarsha)	059	Upz
CHITTAGONG	01	COMILLA	06	HOMNA	060	Upz
CHITTAGONG	01	COMILLA	06	BRAHMANPARA	061	Upz
CHITTAGONG	01	COMILLA	06	BURICHANG	062	Upz
CHITTAGONG	01	COMILLA	06	LAKSHAM MUN.	063	Mun
CHITTAGONG	01	COMILLA	06	NANGALKOT	064	Upz
CHITTAGONG	01	COMILLA	06	LAKSAM	065	Upz
CHITTAGONG	01	COMILLA	06	COMILLA SADAR SOUTH	561	Upz
CHITTAGONG	01	COMILLA	06	MEGHNA	562	Upz
CHITTAGONG	01	COMILLA	06	MONOHORGANJ	563	Upz
CHITTAGONG	01	COMILLA	06	TITAS	564	Upz
CHITTAGONG	01	COMILLA	06	LALMAI	609	Upz
CHITTAGONG	01	COX'S BAZAR	02	COX'S BAZAR S	016	Upz
CHITTAGONG	01	COX'S BAZAR	02	UKHIA	017	Upz
CHITTAGONG	01	COX'S BAZAR	02	RAMU	018	Upz
CHITTAGONG	01	COX'S BAZAR	02	COX'S BAZAR MUN.	019	Mun
CHITTAGONG	01	COX'S BAZAR	02	CHAKARIA	020	Upz
CHITTAGONG	01	COX'S BAZAR	02	KUTUBDIA	021	Upz
CHITTAGONG	01	COX'S BAZAR	02	MAHESHKHALI	022	Upz
CHITTAGONG	01	COX'S BAZAR	02	TEKNAF	023	Upz
CHITTAGONG	01	COX'S BAZAR	02	PEKUA	567	Upz
CHITTAGONG	01	FENI	14	SONAGAZI	131	Upz
CHITTAGONG	01	FENI	14	DAGANBHUIYAN	132	Upz
CHITTAGONG	01	FENI	14	CHHAGALNAIYA	133	Upz
CHITTAGONG	01	FENI	14	PARSHURAM	134	Upz
CHITTAGONG	01	FENI	14	FENI MUN.	135	Mun
CHITTAGONG	01	FENI	14	FENI SADAR	136	Upz
CHITTAGONG	01	FENI	14	FULGAZI	570	Upz
CHITTAGONG	01	KHAGRACHARI	03	KHAGRACHHARI SADAR	024	Upz
CHITTAGONG	01	KHAGRACHARI	03	DIGHINALA	025	Upz
CHITTAGONG	01	KHAGRACHARI	03	MAHALCHARI	026	Upz
CHITTAGONG	01	KHAGRACHARI	03	PANCHHARI	027	Upz
CHITTAGONG	01	KHAGRACHARI	03	MATIRANGA	028	Upz
CHITTAGONG	01	KHAGRACHARI	03	RAMGARH	029	Upz
CHITTAGONG	01	KHAGRACHARI	03	LAKSHMICHHARI	030	Upz
CHITTAGONG	01	KHAGRACHARI	03	MANIKCHARI	031	Upz
CHITTAGONG	01	KHAGRACHARI	03	KHAGRACHARI MU.	032	Mun
CHITTAGONG	01	LAKSHMIPUR	15	LAKSHMIPUR S	137	Upz
CHITTAGONG	01	LAKSHMIPUR	15	RAIPUR-LAK	138	Upz
CHITTAGONG	01	LAKSHMIPUR	15	RAMGANJ	139	Upz
CHITTAGONG	01	LAKSHMIPUR	15	RAMGATI	140	Upz
CHITTAGONG	01	LAKSHMIPUR	15	LAKSHMIPUR MUN.	141	Mun
CHITTAGONG	01	LAKSHMIPUR	15	KOMOLNAGAR	571	Upz
CHITTAGONG	01	NOAKHALI	13	NOAKHALI S (Kabirhat)	123	Upz
CHITTAGONG	01	NOAKHALI	13	SENBAGH	124	Upz
CHITTAGONG	01	NOAKHALI	13	CHATKHIL	125	Upz
CHITTAGONG	01	NOAKHALI	13	NOAKHALI MUN.	126	Mun
CHITTAGONG	01	NOAKHALI	13	BEGUMGANJ	127	Upz
CHITTAGONG	01	NOAKHALI	13	COMPANIGANJ-NOA	128	Upz
CHITTAGONG	01	NOAKHALI	13	HATIYA	129	Upz

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CHITTAGONG	01	NOAKHALI	13	BEGUMGANJ MUN.	130	Mun
CHITTAGONG	01	NOAKHALI	13	SHUBARNACHAR	568	Upz
CHITTAGONG	01	NOAKHALI	13	SONAIMURI	569	Upz
CHITTAGONG	01	NOAKHALI	13	KABIRHAT	580	Upz
CHITTAGONG	01	RANGAMATI	04	BAGAICHHARI	033	Upz
CHITTAGONG	01	RANGAMATI	04	BARKAL	034	Upz
CHITTAGONG	01	RANGAMATI	04	KAWKHALI	035	Upz
CHITTAGONG	01	RANGAMATI	04	JURAICHHARI	036	Upz
CHITTAGONG	01	RANGAMATI	04	LANGADU	037	Upz
CHITTAGONG	01	RANGAMATI	04	NANNERCHAR	038	Upz
CHITTAGONG	01	RANGAMATI	04	RANGAMATI S	039	Upz
CHITTAGONG	01	RANGAMATI	04	BELAICHHARI	040	Upz
CHITTAGONG	01	RANGAMATI	04	KAPTAI	041	Upz
CHITTAGONG	01	RANGAMATI	04	RAJSTHALI	042	Upz
CHITTAGONG	01	RANGAMATI	04	RANGAMATI MUN.	043	Mun
DHAKA	02	DHAKA	16	DHAMRAI	142	Upz
DHAKA	02	DHAKA	16	SAVAR	143	Upz
DHAKA	02	DHAKA	16	KERANIGANJ	144	Upz
DHAKA	02	DHAKA	16	NAWABGANJ	145	Upz
DHAKA	02	DHAKA	16	DOHAR	146	Upz
DHAKA	02	DHAKA	16	DNCC	147	CC
DHAKA	02	DHAKA	16	DSCC	182	CC
DHAKA	02	DHAKA	16	TEJGAON CIRCLE	549	Upz
DHAKA	02	DHAKA	16	SAVAR MUN.	557	Mun
DHAKA	02	FARIDPUR	23	FARIDPUR S	196	Upz
DHAKA	02	FARIDPUR	23	BHANGA	197	Upz
DHAKA	02	FARIDPUR	23	NAGARKANDA (Salta)	198	Upz
DHAKA	02	FARIDPUR	23	SADARPUR	199	Upz
DHAKA	02	FARIDPUR	23	FARIDPUR MUN.	200	Mun
DHAKA	02	FARIDPUR	23	ALFADANGA	201	Upz
DHAKA	02	FARIDPUR	23	MADHUKHALI	202	Upz
DHAKA	02	FARIDPUR	23	BOALMARI	203	Upz
DHAKA	02	FARIDPUR	23	CHAR BHADRASAN	204	Upz
DHAKA	02	FARIDPUR	23	SALTHA	612	Upz
DHAKA	02	GAZIPUR	21	GAZIPUR S / Joydevpur	176	Upz
DHAKA	02	GAZIPUR	21	SREEPUR	177	Upz
DHAKA	02	GAZIPUR	21	KALIAKAIR	178	Upz
DHAKA	02	GAZIPUR	21	KAPASIA	179	Upz
DHAKA	02	GAZIPUR	21	KALIGANJ-GAZ	180	Upz
DHAKA	02	GAZIPUR	21	GAZIPUR CC	181	CC
DHAKA	02	GOPALGANJ	27	GOPALGANJ S	222	Upz
DHAKA	02	GOPALGANJ	27	KASHIANI	223	Upz
DHAKA	02	GOPALGANJ	27	KOTALIPARA	224	Upz
DHAKA	02	GOPALGANJ	27	MUKSUDPUR	225	Upz
DHAKA	02	GOPALGANJ	27	TUNGIPARA	226	Upz
DHAKA	02	GOPALGANJ	27	GOPALGANJ MUN.	227	Mun
DHAKA	02	KISHOREGANJ	29	PAKUNDIA	243	Upz
DHAKA	02	KISHOREGANJ	29	KISHOREGANJ S	244	Upz
DHAKA	02	KISHOREGANJ	29	KARIMGANJ	245	Upz
DHAKA	02	KISHOREGANJ	29	KISHOREGANJ MUN.	246	Mun
DHAKA	02	KISHOREGANJ	29	ASTAGRAM	247	Upz
DHAKA	02	KISHOREGANJ	29	MITHAMAIN	248	Upz
DHAKA	02	KISHOREGANJ	29	BAJITPUR	249	Upz

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DHAKA	02	KISHOREGANJ	29	BHAIRAB	250	Upz
DHAKA	02	KISHOREGANJ	29	HOSSAINPUR	251	Upz
DHAKA	02	KISHOREGANJ	29	ITNA	252	Upz
DHAKA	02	KISHOREGANJ	29	KATIADI	253	Upz
DHAKA	02	KISHOREGANJ	29	NIKLI	254	Upz
DHAKA	02	KISHOREGANJ	29	TARAIL	255	Upz
DHAKA	02	KISHOREGANJ	29	KULIARCHAR	256	Upz
DHAKA	02	KISHOREGANJ	29	BHAIRAB MUN.	257	Mun
DHAKA	02	KISHOREGANJ	29	BAJITPUR MUN.	258	Mun
DHAKA	02	MADARIPUR	25	MADARIPUR S	210	Upz
DHAKA	02	MADARIPUR	25	KALKINI	211	Upz
DHAKA	02	MADARIPUR	25	RAJOIR	212	Upz
DHAKA	02	MADARIPUR	25	SHIBCHAR	213	Upz
DHAKA	02	MADARIPUR	25	MADARIPUR MUN.	214	Mun
DHAKA	02	MADARIPUR	25	SHIBCHAR MUN.	558	Mun
DHAKA	02	MANIKGANJ	17	MANIKGANJ S	148	Upz
DHAKA	02	MANIKGANJ	17	GHIOR	149	Upz
DHAKA	02	MANIKGANJ	17	SATURIA	150	Upz
DHAKA	02	MANIKGANJ	17	SINGAIR	151	Upz
DHAKA	02	MANIKGANJ	17	SHIVALAYA	152	Upz
DHAKA	02	MANIKGANJ	17	HARIRAMPUR	153	Upz
DHAKA	02	MANIKGANJ	17	DAULATPUR	154	Upz
DHAKA	02	MANIKGANJ	17	MANIKGANJ MUN.	155	Mun
DHAKA	02	MUNSHIGANJ	20	SERAJDIKHAN	169	Upz
DHAKA	02	MUNSHIGANJ	20	TONGIBARI	170	Upz
DHAKA	02	MUNSHIGANJ	20	SREENAGAR	171	Upz
DHAKA	02	MUNSHIGANJ	20	MUNSHIGANJ S	172	Upz
DHAKA	02	MUNSHIGANJ	20	LOHAJANG	173	Upz
DHAKA	02	MUNSHIGANJ	20	MUNSHIGANJ MUN.	174	Mun
DHAKA	02	MUNSHIGANJ	20	GAZARIA	175	Upz
DHAKA	02	NARAYANGANJ	19	NARAYANGANJ S	163	Upz
DHAKA	02	NARAYANGANJ	19	ARAIHAZAR	164	Upz
DHAKA	02	NARAYANGANJ	19	SONARGAON	165	Upz
DHAKA	02	NARAYANGANJ	19	BANDAR	166	Upz
DHAKA	02	NARAYANGANJ	19	RUPGANJ	167	Upz
DHAKA	02	NARAYANGANJ	19	NARAYANGANJ CC	168	CC
DHAKA	02	NARSINGDI	18	MONOHARDI	156	Upz
DHAKA	02	NARSINGDI	18	SHIBPUR	157	Upz
DHAKA	02	NARSINGDI	18	NARSINGDI S	158	Upz
DHAKA	02	NARSINGDI	18	BELABO	159	Upz
DHAKA	02	NARSINGDI	18	PALASH	160	Upz
DHAKA	02	NARSINGDI	18	RAIPUR-NAR	161	Upz
DHAKA	02	NARSINGDI	18	NARSHINGDHI MUN.	162	Mun
DHAKA	02	RAJBARI	24	RJB_SADAR	205	Upz
DHAKA	02	RAJBARI	24	BALIAKANDA	206	Upz
DHAKA	02	RAJBARI	24	GOALUNDO	207	Upz
DHAKA	02	RAJBARI	24	PANGSA	208	Upz
DHAKA	02	RAJBARI	24	RAJBARI MUN.	209	Mun
DHAKA	02	RAJBARI	24	KALUKHALI	583	Upz
DHAKA	02	SARIATPUR	26	BHEDARGANJ	215	Upz
DHAKA	02	SARIATPUR	26	DAMODYA	216	Upz
DHAKA	02	SARIATPUR	26	GOSAIRHAT	217	Upz
DHAKA	02	SARIATPUR	26	NARIA	218	Upz

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DHAKA	02	SARIATPUR	26	SAR_SADAR / Palong	219	Upz
DHAKA	02	SARIATPUR	26	ZANJIRA	220	Upz
DHAKA	02	SARIATPUR	26	SARIATPUR MUN.	221	Mun
DHAKA	02	SARIATPUR	26	SHAKHIPUR	613	Upz
DHAKA	02	TANGAIL	22	KALIHATI	183	Upz
DHAKA	02	TANGAIL	22	GHATAIL	184	Upz
DHAKA	02	TANGAIL	22	BHUAPUR	185	Upz
DHAKA	02	TANGAIL	22	DELDUAR	186	Upz
DHAKA	02	TANGAIL	22	TANGAIL MUN.	187	Mun
DHAKA	02	TANGAIL	22	TAN_SADAR	188	Upz
DHAKA	02	TANGAIL	22	BASAIL	189	Upz
DHAKA	02	TANGAIL	22	MADHUPUR	190	Upz
DHAKA	02	TANGAIL	22	MIRZAPUR	191	Upz
DHAKA	02	TANGAIL	22	NAGARPUR	192	Upz
DHAKA	02	TANGAIL	22	GOPALPUR	193	Upz
DHAKA	02	TANGAIL	22	SHAKHIPUR	194	Upz
DHAKA	02	TANGAIL	22	GOPALPUR MUN.	195	Mun
DHAKA	02	TANGAIL	22	MADHUPUR MUN.	559	Mun
DHAKA	02	TANGAIL	22	DHANBARI	572	Upz
KHULNA	03	BAGERHAT	34	BAGERHAT S	295	Upz
KHULNA	03	BAGERHAT	34	CHITALMARI	296	Upz
KHULNA	03	BAGERHAT	34	FAKIRHAT	297	Upz
KHULNA	03	BAGERHAT	34	KACHUA-BAGERHA	298	Upz
KHULNA	03	BAGERHAT	34	MOLLAHAT	299	Upz
KHULNA	03	BAGERHAT	34	MORRELGANJ	300	Upz
KHULNA	03	BAGERHAT	34	RAMPAL	301	Upz
KHULNA	03	BAGERHAT	34	MONGLA	302	Upz
KHULNA	03	BAGERHAT	34	SHARANKHOLA	303	Upz
KHULNA	03	BAGERHAT	34	BAGERHAT MUN.	304	Mun
KHULNA	03	BAGERHAT	34	MONGLA MUN.	305	Mun
KHULNA	03	CHUADANGA	41	ALAMDANGA	351	Upz
KHULNA	03	CHUADANGA	41	CHU_SADAR	352	Upz
KHULNA	03	CHUADANGA	41	DAMURHUDA	353	Upz
KHULNA	03	CHUADANGA	41	JIBANNAGAR	354	Upz
KHULNA	03	CHUADANGA	41	CHUADANGA MUN.	355	Mun
KHULNA	03	CHUADANGA	41	ALAMDANGA MUN.	356	Mun
KHULNA	03	CHUADANGA	41	DARSANA MUN.	552	Mun
KHULNA	03	CHUADANGA	41	JIBANNAGAR MUN.	565	Mun
KHULNA	03	JESSORE	36	JES_SADAR	314	Upz
KHULNA	03	JESSORE	36	JHIKARGACHA	315	Upz
KHULNA	03	JESSORE	36	ABHOYNAGAR	316	Upz
KHULNA	03	JESSORE	36	BAGHERPARA	317	Upz
KHULNA	03	JESSORE	36	CHOUGACHA	318	Upz
KHULNA	03	JESSORE	36	SARSHA	319	Upz
KHULNA	03	JESSORE	36	MANIRAMPUR	320	Upz
KHULNA	03	JESSORE	36	KESHABPUR	321	Upz
KHULNA	03	JESSORE	36	JESSORE MUN.	322	Mun
KHULNA	03	JHENAIDAH	39	JHE_SADAR	333	Upz
KHULNA	03	JHENAIDAH	39	HARINAKUNDA	334	Upz
KHULNA	03	JHENAIDAH	39	KALIGANJ_JHEN.	335	Upz
KHULNA	03	JHENAIDAH	39	KOTCHANDPUR	336	Upz
KHULNA	03	JHENAIDAH	39	MOHESHPUR	337	Upz
KHULNA	03	JHENAIDAH	39	SAILAKUPA	338	Upz

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KHULNA	03	JHENAIDAH	39	JHENAIDAH MUN.	339	Mun
KHULNA	03	JHENAIDAH	39	KOTCHANDPUR MUN.	340	Mun
KHULNA	03	JHENAIDAH	39	MOHESHPUR MUN.	341	Mun
KHULNA	03	JHENAIDAH	39	KALIGANJ MUN.	582	Mun
KHULNA	03	JHENAIDAH	39	SAILAKUPA MUN.	584	Mun
KHULNA	03	KHULNA	33	PAIKGACHA	285	Upz
KHULNA	03	KHULNA	33	KOIRA	286	Upz
KHULNA	03	KHULNA	33	DACOPE	287	Upz
KHULNA	03	KHULNA	33	BATIAGHATA	288	Upz
KHULNA	03	KHULNA	33	DUMURIA	289	Upz
KHULNA	03	KHULNA	33	PHULTALA	290	Upz
KHULNA	03	KHULNA	33	DIGHALIA	291	Upz
KHULNA	03	KHULNA	33	RUPSHA	292	Upz
KHULNA	03	KHULNA	33	TEROKHADA	293	Upz
KHULNA	03	KHULNA	33	KHULNA CC.	294	CC
KHULNA	03	KUSHTIA	40	KUSHTIA MUN.	342	Mun
KHULNA	03	KUSHTIA	40	BHERAMARA	343	Upz
KHULNA	03	KUSHTIA	40	DAULATPUR-KUSH	344	Upz
KHULNA	03	KUSHTIA	40	KHOKSA	345	Upz
KHULNA	03	KUSHTIA	40	KUMARKHALI	346	Upz
KHULNA	03	KUSHTIA	40	KUS_SADAR	347	Upz
KHULNA	03	KUSHTIA	40	MIRPUR	348	Upz
KHULNA	03	KUSHTIA	40	BHERAMARA MUN.	349	Mun
KHULNA	03	KUSHTIA	40	KUMARKHALI MUN.	350	Mun
KHULNA	03	MAGURA	38	MAG_SADAR	328	Upz
KHULNA	03	MAGURA	38	MOHAMMADPUR	329	Upz
KHULNA	03	MAGURA	38	SALIKHA	330	Upz
KHULNA	03	MAGURA	38	SREEPUR-MAG.	331	Upz
KHULNA	03	MAGURA	38	MAGURA MUN.	332	Mun
KHULNA	03	MEHERPUR	42	MER_SADAR	357	Upz
KHULNA	03	MEHERPUR	42	GANGNI	358	Upz
KHULNA	03	MEHERPUR	42	MEHERPUR MUN.	359	Mun
KHULNA	03	MEHERPUR	42	MUJIBNAGAR	551	Upz
KHULNA	03	NARAIL	37	NRI_SADAR	323	Upz
KHULNA	03	NARAIL	37	KALIA	324	Upz
KHULNA	03	NARAIL	37	LOHAGARA_NARAI	325	Upz
KHULNA	03	NARAIL	37	NARAIL MUN.	326	Mun
KHULNA	03	NARAIL	37	KALIA MUN.	327	Mun
KHULNA	03	NARAIL	37	NARAGATI	615	Upz
KHULNA	03	SATKHIRA	35	SATKHIRA MUN.	306	Mun
KHULNA	03	SATKHIRA	35	ASSASUNI	307	Upz
KHULNA	03	SATKHIRA	35	DEBHATTA	308	Upz
KHULNA	03	SATKHIRA	35	KALAROA	309	Upz
KHULNA	03	SATKHIRA	35	KALIGANJ_SAT.	310	Upz
KHULNA	03	SATKHIRA	35	SAT_SADAR	311	Upz
KHULNA	03	SATKHIRA	35	SHYAMNAGAR	312	Upz
KHULNA	03	SATKHIRA	35	TALA	313	Upz
MYMENSINGH	08	JAMALPUR	31	JAMALPUR S	271	Upz
MYMENSINGH	08	JAMALPUR	31	MELANDAHA	272	Upz
MYMENSINGH	08	JAMALPUR	31	DEWANGANJ	273	Upz
MYMENSINGH	08	JAMALPUR	31	JAMALPUR MUN.	274	Mun
MYMENSINGH	08	JAMALPUR	31	ISLAMPUR	275	Upz
MYMENSINGH	08	JAMALPUR	31	SARISHABARI	276	Upz

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MYMENSINGH	08	JAMALPUR	31	BAKSIGANJ	277	Upz
MYMENSINGH	08	JAMALPUR	31	MADARGANJ	278	Upz
MYMENSINGH	08	JAMALPUR	31	SARISHABARI MUN.	554	Mun
MYMENSINGH	08	MYMENSINGH	28	MYMENSINGH S.	226	Upz
MYMENSINGH	08	MYMENSINGH	28	TRISHAL	229	Upz
MYMENSINGH	08	MYMENSINGH	28	MUKTAGACHA	230	Upz
MYMENSINGH	08	MYMENSINGH	28	GAFFARGAON	231	Upz
MYMENSINGH	08	MYMENSINGH	28	GAURIPUR	232	Upz
MYMENSINGH	08	MYMENSINGH	28	NANDAIL	233	Upz
MYMENSINGH	08	MYMENSINGH	28	MYMENSINGH CC.	234	CC
MYMENSINGH	08	MYMENSINGH	28	HALUAGHAT	235	Upz
MYMENSINGH	08	MYMENSINGH	28	ISWARGANJ	236	Upz
MYMENSINGH	08	MYMENSINGH	28	PHULPUR	237	Upz
MYMENSINGH	08	MYMENSINGH	28	BHALUKA	238	Upz
MYMENSINGH	08	MYMENSINGH	28	PHULBARI	239	Upz
MYMENSINGH	08	MYMENSINGH	28	MUKTAGACHA MUN.	240	Mun
MYMENSINGH	08	MYMENSINGH	28	GOURIPUR MUN.	241	Mun
MYMENSINGH	08	MYMENSINGH	28	DHOBAURA	242	Upz
MYMENSINGH	08	MYMENSINGH	28	TARA KHANDA	614	Upz
MYMENSINGH	08	NETROKONA	30	NET_SADAR	259	Upz
MYMENSINGH	08	NETROKONA	30	PURBADHALA	260	Upz
MYMENSINGH	08	NETROKONA	30	ATPARA	261	Upz
MYMENSINGH	08	NETROKONA	30	BARHATTA	262	Upz
MYMENSINGH	08	NETROKONA	30	DURGAPUR_NET.	263	Upz
MYMENSINGH	08	NETROKONA	30	KALIAJURI	264	Upz
MYMENSINGH	08	NETROKONA	30	KALMAKANDA	265	Upz
MYMENSINGH	08	NETROKONA	30	KENDUA	266	Upz
MYMENSINGH	08	NETROKONA	30	MADAN	267	Upz
MYMENSINGH	08	NETROKONA	30	MOHANGANJ	268	Upz
MYMENSINGH	08	NETROKONA	30	NETROKONA MUN.	269	Mun
MYMENSINGH	08	NETROKONA	30	MOHONGANJ MUN.	270	Mun
MYMENSINGH	08	SHERPUR	32	SER_SADAR	279	Upz
MYMENSINGH	08	SHERPUR	32	NALITABARI	280	Upz
MYMENSINGH	08	SHERPUR	32	SHERPUR MUN.	281	Mun
MYMENSINGH	08	SHERPUR	32	JHENAIGATI	282	Upz
MYMENSINGH	08	SHERPUR	32	NAKHLA	283	Upz
MYMENSINGH	08	SHERPUR	32	SREEBORDI	284	Upz
MYMENSINGH	08	SHERPUR	32	NALITABARI MUN.	575	Mun
RAJSHAHI	05	BOGRA	55	BOG_SADAR	461	Upz
RAJSHAHI	05	BOGRA	55	GABTALI	462	Upz
RAJSHAHI	05	BOGRA	55	KAHALOO	463	Upz
RAJSHAHI	05	BOGRA	55	SHERPUR	464	Upz
RAJSHAHI	05	BOGRA	55	SARIAKANDI	465	Upz
RAJSHAHI	05	BOGRA	55	ADAMDIGHI	466	Upz
RAJSHAHI	05	BOGRA	55	BOG_SHIBGANJ	467	Upz
RAJSHAHI	05	BOGRA	55	DUBCHACHIA	468	Upz
RAJSHAHI	05	BOGRA	55	SONATALA	469	Upz
RAJSHAHI	05	BOGRA	55	BOGRA MUN.	470	Mun
RAJSHAHI	05	BOGRA	55	DHUNAT	471	Upz
RAJSHAHI	05	BOGRA	55	NANDIGRAM	472	Upz
RAJSHAHI	05	BOGRA	55	SHERPUR MUN. (BOG)	473	Mun
RAJSHAHI	05	BOGRA	55	SHAHJAHANPUR	553	Upz
RAJSHAHI	05	BOGRA	55	SHANTAHAR MUN.	601	Mun

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RAJSHAHI	05	BOGRA	55	DUBCHACHIA MUN.	602	Mun
RAJSHAHI	05	JOYPURHAT	56	JOY_SADAR	474	Upz
RAJSHAHI	05	JOYPURHAT	56	KHETLAL	475	Upz
RAJSHAHI	05	JOYPURHAT	56	PANCHABIBI	476	Upz
RAJSHAHI	05	JOYPURHAT	56	KALAI	477	Upz
RAJSHAHI	05	JOYPURHAT	56	AKKELPUR	478	Upz
RAJSHAHI	05	JOYPURHAT	56	JOYPURHAT MUN.	479	Mun
RAJSHAHI	05	JOYPURHAT	56	PANCHABIBI MUN.	603	Mun
RAJSHAHI	05	JOYPURHAT	56	AKKELPUR MUN.	604	Mun
RAJSHAHI	05	NATORE	51	BAGATIPARA	421	Upz
RAJSHAHI	05	NATORE	51	BARAIGRAM	422	Upz
RAJSHAHI	05	NATORE	51	GURUDASPUR	423	Upz
RAJSHAHI	05	NATORE	51	LALPUR	424	Upz
RAJSHAHI	05	NATORE	51	NAT_SADAR	425	Upz
RAJSHAHI	05	NATORE	51	SINGRA	426	Upz
RAJSHAHI	05	NATORE	51	NATORE MUN.	427	Mun
RAJSHAHI	05	NATORE	51	BANPARA MUN.	595	Mun
RAJSHAHI	05	NATORE	51	NALDANGA	617	Upz
RAJSHAHI	05	NOAGOAN	52	NAO_SADAR	428	Upz
RAJSHAHI	05	NOAGOAN	52	RANINAGAR	429	Upz
RAJSHAHI	05	NOAGOAN	52	ATRAI	430	Upz
RAJSHAHI	05	NOAGOAN	52	MANDA	431	Upz
RAJSHAHI	05	NOAGOAN	52	NOAGOAN MUN.	432	Mun
RAJSHAHI	05	NOAGOAN	52	BADALGACHI	433	Upz
RAJSHAHI	05	NOAGOAN	52	DHAMOIRHAT	434	Upz
RAJSHAHI	05	NOAGOAN	52	MAHADEVPUR	435	Upz
RAJSHAHI	05	NOAGOAN	52	NIAMATPUR	436	Upz
RAJSHAHI	05	NOAGOAN	52	PATNITOLA	437	Upz
RAJSHAHI	05	NOAGOAN	52	PORSHA	438	Upz
RAJSHAHI	05	NOAGOAN	52	SHAPAHAR	439	Upz
RAJSHAHI	05	NOAGOAN	52	DHAMOIRHAT MUN.	596	Mun
RAJSHAHI	05	NOWABGANJ	50	NAW_SADAR	415	Upz
RAJSHAHI	05	NOWABGANJ	50	BHOLAHAT	416	Upz
RAJSHAHI	05	NOWABGANJ	50	GOMASTAPUR	417	Upz
RAJSHAHI	05	NOWABGANJ	50	NACHOLE	418	Upz
RAJSHAHI	05	NOWABGANJ	50	NAB_SHIBGANJ	419	Upz
RAJSHAHI	05	NOWABGANJ	50	NOWABGANJ MUN.	420	Mun
RAJSHAHI	05	NOWABGANJ	50	SHIBGANJ MUN.	594	Mun
RAJSHAHI	05	PABNA	53	ISWARDI	440	Upz
RAJSHAHI	05	PABNA	53	SANTHIA	441	Upz
RAJSHAHI	05	PABNA	53	ATGHORIA	442	Upz
RAJSHAHI	05	PABNA	53	BERA	443	Upz
RAJSHAHI	05	PABNA	53	CHATMOHAR	444	Upz
RAJSHAHI	05	PABNA	53	SUJANAGAR	445	Upz
RAJSHAHI	05	PABNA	53	FARIDPUR	446	Upz
RAJSHAHI	05	PABNA	53	PABNA MUN.	447	Mun
RAJSHAHI	05	PABNA	53	PAB_SADAR	448	Upz
RAJSHAHI	05	PABNA	53	BHANGOORA	449	Upz
RAJSHAHI	05	PABNA	53	ISWARDI MUN.	450	Mun
RAJSHAHI	05	PABNA	53	BERA MUN.	597	Mun
RAJSHAHI	05	PABNA	53	SUJANAGAR MUN.	598	Mun
RAJSHAHI	05	RAJSHAHI	49	PABA	405	Upz
RAJSHAHI	05	RAJSHAHI	49	PUTHIA	406	Upz

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RAJSHAHI	05	RAJSHAHI	49	CHARGHAT	407	Upz
RAJSHAHI	05	RAJSHAHI	49	BAGMARA	408	Upz
RAJSHAHI	05	RAJSHAHI	49	GODAGARI	409	Upz
RAJSHAHI	05	RAJSHAHI	49	DURGAPUR_RAJ.	410	Upz
RAJSHAHI	05	RAJSHAHI	49	MOHANPUR	411	Upz
RAJSHAHI	05	RAJSHAHI	49	TANORE	412	Upz
RAJSHAHI	05	RAJSHAHI	49	BAGHA	413	Upz
RAJSHAHI	05	RAJSHAHI	49	RAJSHAHI CC.	414	CC
RAJSHAHI	05	RAJSHAHI	49	GODAGARI MUN.	580	Mun
RAJSHAHI	05	RAJSHAHI	49	NAWHATA MUN.	591	Mun
RAJSHAHI	05	RAJSHAHI	49	TAHIRPUR MUN.	592	Mun
RAJSHAHI	05	RAJSHAHI	49	DURGAPUR MUN.	593	Mun
RAJSHAHI	05	SIRAJGANJ	54	SIRAJGANJ MUN.	451	Mun
RAJSHAHI	05	SIRAJGANJ	54	KAMARKANDI	452	Upz
RAJSHAHI	05	SIRAJGANJ	54	RAIGANJ	453	Upz
RAJSHAHI	05	SIRAJGANJ	54	SHAHZADPUR	454	Upz
RAJSHAHI	05	SIRAJGANJ	54	ULLAPARA	455	Upz
RAJSHAHI	05	SIRAJGANJ	54	SRJ_SADAR	456	Upz
RAJSHAHI	05	SIRAJGANJ	54	BELKUCHI	457	Upz
RAJSHAHI	05	SIRAJGANJ	54	CHOWHALI	458	Upz
RAJSHAHI	05	SIRAJGANJ	54	KAZIPUR	459	Upz
RAJSHAHI	05	SIRAJGANJ	54	TARASH	460	Upz
RAJSHAHI	05	SIRAJGANJ	54	ULLAPARA MUN.	599	Mun
RAJSHAHI	05	SIRAJGANJ	54	KAZIPUR MUN.	600	Mun
RANGPUR	07	DINAJPUR	62	BIRAMPUR MUN.	586	Mun
RANGPUR	07	DINAJPUR	62	HAKIMPUR	521	Upz
RANGPUR	07	DINAJPUR	62	BIROLE	522	Upz
RANGPUR	07	DINAJPUR	62	CHIRIRBANDAR	523	Upz
RANGPUR	07	DINAJPUR	62	PARBATIPUR	524	Upz
RANGPUR	07	DINAJPUR	62	BIRGANJ	525	Upz
RANGPUR	07	DINAJPUR	62	DIN_SADAR	526	Upz
RANGPUR	07	DINAJPUR	62	BIRAMPUR	527	Upz
RANGPUR	07	DINAJPUR	62	FULBARI	528	Upz
RANGPUR	07	DINAJPUR	62	GHORAGHAT	529	Upz
RANGPUR	07	DINAJPUR	62	KAHAROLE	530	Upz
RANGPUR	07	DINAJPUR	62	KHANSAMA	531	Upz
RANGPUR	07	DINAJPUR	62	DIN_NAWABGANJ	532	Upz
RANGPUR	07	DINAJPUR	62	BOCHAGANJ	533	Upz
RANGPUR	07	DINAJPUR	62	DINAJPUR MUN.	534	Mun
RANGPUR	07	DINAJPUR	62	FULBARI MUN.	535	Mun
RANGPUR	07	DINAJPUR	62	PARBATIPUR MUN.	536	Mun
RANGPUR	07	DINAJPUR	62	SETABGANJ MUN.	587	Mun
RANGPUR	07	GAIBANDHA	58	FULCHARI	489	Upz
RANGPUR	07	GAIBANDHA	58	GAI_SADAR	490	Upz
RANGPUR	07	GAIBANDHA	58	GOBINDAGANJ	491	Upz
RANGPUR	07	GAIBANDHA	58	PALASHBARI	492	Upz
RANGPUR	07	GAIBANDHA	58	SADULLAPUR	493	Upz
RANGPUR	07	GAIBANDHA	58	SUGATHA	494	Upz
RANGPUR	07	GAIBANDHA	58	SUNDARGANJ	495	Upz
RANGPUR	07	GAIBANDHA	58	GAIBANDHA MUN.	496	Mun
RANGPUR	07	GAIBANDHA	58	GOBINDAGANJ MUN.	605	Mun
RANGPUR	07	KURIGRAM	60	FHULBARI	505	Upz
RANGPUR	07	KURIGRAM	60	ULIPUR	508	Upz

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RANGPUR	07	KURIGRAM	60	KUR_SADAR	507	Upz
RANGPUR	07	KURIGRAM	60	BHURANGAMARI	508	Upz
RANGPUR	07	KURIGRAM	60	CHAR RAJIBPUR	509	Upz
RANGPUR	07	KURIGRAM	60	CHILMARI	510	Upz
RANGPUR	07	KURIGRAM	60	NAGESWARI	511	Upz
RANGPUR	07	KURIGRAM	60	RAJARHAT	512	Upz
RANGPUR	07	KURIGRAM	60	ROWMARI	513	Upz
RANGPUR	07	KURIGRAM	60	KURIGRAM MUN.	514	Mun
RANGPUR	07	LALMONIRHAT	61	LAL_SADAR	515	Upz
RANGPUR	07	LALMONIRHAT	61	ADITMARI	516	Upz
RANGPUR	07	LALMONIRHAT	61	HATIBANDHA	517	Upz
RANGPUR	07	LALMONIRHAT	61	KALIGANJ-LAL	518	Upz
RANGPUR	07	LALMONIRHAT	61	PATGRAM	519	Upz
RANGPUR	07	LALMONIRHAT	61	LALMONIRHAT MUN.	520	Mun
RANGPUR	07	LALMONIRHAT	61	PATGRAM MUN.	606	Mun
RANGPUR	07	NILPHAMARI	59	NIL_SADAR	487	Upz
RANGPUR	07	NILPHAMARI	59	DOMAR	498	Upz
RANGPUR	07	NILPHAMARI	59	DIMLA	499	Upz
RANGPUR	07	NILPHAMARI	59	JALDHAKA	500	Upz
RANGPUR	07	NILPHAMARI	59	KISHOREGANJ	501	Upz
RANGPUR	07	NILPHAMARI	59	SAIDPUR MUN.	502	Mun
RANGPUR	07	NILPHAMARI	59	NILPHAMARI MUN.	503	Mun
RANGPUR	07	NILPHAMARI	59	SAIDPUR	504	Upz
RANGPUR	07	PANCHAGHARH	64	PAN_SADAR	543	Upz
RANGPUR	07	PANCHAGHARH	64	ATWARI	544	Upz
RANGPUR	07	PANCHAGHARH	64	BODA	545	Upz
RANGPUR	07	PANCHAGHARH	64	DEBIGANJ	546	Upz
RANGPUR	07	PANCHAGHARH	64	TETULIA	547	Upz
RANGPUR	07	PANCHAGHARH	64	PANCHAGARH MUN.	548	Mun
RANGPUR	07	RANGPUR	57	GANGACHARA	480	Upz
RANGPUR	07	RANGPUR	57	TARAGANJ	481	Upz
RANGPUR	07	RANGPUR	57	RANGPUR CC	482	CC
RANGPUR	07	RANGPUR	57	RANG_SADAR	483	Upz
RANGPUR	07	RANGPUR	57	PIRGACHA	484	Upz
RANGPUR	07	RANGPUR	57	KAUNIA	485	Upz
RANGPUR	07	RANGPUR	57	MITHAPUKUR	486	Upz
RANGPUR	07	RANGPUR	57	BADARGANJ	487	Upz
RANGPUR	07	RANGPUR	57	PIRGANJ - RANG	488	Upz
RANGPUR	07	THAKURGOAN	63	PIRGANJ - THAK	537	Upz
RANGPUR	07	THAKURGOAN	63	THA_SADAR	538	Upz
RANGPUR	07	THAKURGOAN	63	BALIADANGI	539	Upz
RANGPUR	07	THAKURGOAN	63	THAKURGAON MUN.	540	Mun
RANGPUR	07	THAKURGOAN	63	HARIPUR	541	Upz
RANGPUR	07	THAKURGOAN	63	RANISHANKAIL	542	Upz
RANGPUR	07	THAKURGOAN	63	PIRGANJ MUN.	607	Mun
SYLHET	06	HABIGANJ	12	HABIGANJ S	114	Upz
SYLHET	06	HABIGANJ	12	NABIGANJ	115	Upz
SYLHET	06	HABIGANJ	12	AZMIRIGANJ	116	Upz
SYLHET	06	HABIGANJ	12	BANIACHONG	117	Upz
SYLHET	06	HABIGANJ	12	LAKHAI	118	Upz
SYLHET	06	HABIGANJ	12	BAHUBAL	119	Upz
SYLHET	06	HABIGANJ	12	CHUNARUGHAT	120	Upz
SYLHET	06	HABIGANJ	12	MADHABPUR	121	Upz

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SYLHET	06	HABIGANJ	12	MADHABPUR MUN	588	Mun
SYLHET	06	HABIGANJ	12	HABIGANJ MUN	122	Mun
SYLHET	06	HABIGANJ	12	SAYESTAGANJ	611	Upz
SYLHET	06	MOULVI BAZAR	11	MAULVIBAZAR S	106	Upz
SYLHET	06	MOULVI BAZAR	11	BARLEKHA	107	Upz
SYLHET	06	MOULVI BAZAR	11	KULAURA	108	Upz
SYLHET	06	MOULVI BAZAR	11	RAJNAGAR	109	Upz
SYLHET	06	MOULVI BAZAR	11	KAMALGANJ	110	Upz
SYLHET	06	MOULVI BAZAR	11	SREEMANGAL	111	Upz
SYLHET	06	MOULVI BAZAR	11	MOULVIBAZAR MU.	112	Mun
SYLHET	06	MOULVI BAZAR	11	SREEMANGAL MUN.	113	Mun
SYLHET	06	MOULVI BAZAR	11	JURRI	577	Upz
SYLHET	06	MOULVI BAZAR	11	BARLEKHA MUN	589	Mun
SYLHET	06	SUNAMGANJ	10	SUNAMGANJ S	095	Upz
SYLHET	06	SUNAMGANJ	10	BISWAMVARPUR	096	Upz
SYLHET	06	SUNAMGANJ	10	CHHATAK	097	Upz
SYLHET	06	SUNAMGANJ	10	DERAI	098	Upz
SYLHET	06	SUNAMGANJ	10	DHARMAPASHA	099	Upz
SYLHET	06	SUNAMGANJ	10	DOWARABAZAR	100	Upz
SYLHET	06	SUNAMGANJ	10	JAGANNATHPUR	101	Upz
SYLHET	06	SUNAMGANJ	10	JAMALGANJ	102	Upz
SYLHET	06	SUNAMGANJ	10	SULLAH	103	Upz
SYLHET	06	SUNAMGANJ	10	TAHIRPUR	104	Upz
SYLHET	06	SUNAMGANJ	10	SUNAMGANJ MUN.	105	Mun
SYLHET	06	SUNAMGANJ	10	Sunamganj	578	Upz
SYLHET	06	SYLHET	09	BALAGANJ	083	Upz
SYLHET	06	SYLHET	09	BISWANATH	084	Upz
SYLHET	06	SYLHET	09	SYLHET S	085	Upz
SYLHET	06	SYLHET	09	BEANIBAZAR	086	Upz
SYLHET	06	SYLHET	09	COMPANIGANJ-SYL	087	Upz
SYLHET	06	SYLHET	09	FENCHUGANJ	088	Upz
SYLHET	06	SYLHET	09	GOLABGANJ	089	Upz
SYLHET	06	SYLHET	09	GOWAINGHAT	090	Upz
SYLHET	06	SYLHET	09	JAINTIAPUR	091	Upz
SYLHET	06	SYLHET	09	ZAKIGANJ	092	Upz
SYLHET	06	SYLHET	09	KANAIGHAT	093	Upz
SYLHET	06	SYLHET	09	SYLHET CC.	094	CC
SYLHET	06	SYLHET	09	DASKHIN SURMA	579	Upz
SYLHET	06	SYLHET	09	OSMANI NAGAR	610	Upz